ANNALS of ALLERGY

Published by

The American College of Allergists

VOLUME 16

January through December, 1958

Printed in U.S.A.

Contents for January-February, 1958

Contents for March-April, 1958

Because of the backlog of papers and the need for every possible page for text, the Editorials, Papers of Interest and Book Reviews have been omitted from this issue. They will re-appear as space becomes available and the time between submission of manuscripts and their appearance in print can be reduced to a reasonable period.

Contents for May-June, 1958

Contents for July-August, 1958

Contents for September-October, 1958

Contents for November-December, 1958

ANNALS of ALLERGY

Published by
The American College of Allergists

Volume 16 January-February, 1958 Number 1

OBSERVATIONS ON THE DETECTION OF SERUM PROTEIN ABNORMALITIES IN ASTHMATIC CHILDREN

HAROLD S. TUFT, M.D., F.A.C.A.
Denver, Colorado

CHANGES in the levels of electrophoretic serum fractions were found in cases of chronic intractable asthma of childhood.[1] Elevation of gamma globulin was a prominent feature of these changes. This component is known to be elevated in hepatitis[2,4] and the elevations to influence the results of what are commonly known as liver function tests.[3,5,6] A study of these tests was performed on asthmatic children in order to determine their value in detecting protein abnormalities. Allergy textbooks[7,8] assert that liver disease sometimes accompanies chronic asthma, and this study was designed also to differentiate actual liver disease from the changes solely due to the protein abnormalities.

MATERIALS AND METHODS

The panel of tests consisted of cephalin cholesterol flocculation,[9] thymol turbidity,[10] thymol flocculation,[11] zinc turbidity,[3] and zinc flocculation.[3] The colloidal gold test was run early in the course of the study but abandoned when it became apparent that the value of the test would not be proportionate to the increased time and effort it required when compared to the cephalin flocculation test which is produced by the same mechanism.

The cephalin flocculation test and thymol turbidity and flocculation tests depend upon the ability of serum proteins to form complexes with other colloidal particles at certain pH ranges. Gamma globulin prepared by Tiselius electrophoresis always causes flocculation of the cephalin cholesterol mixture without regard to the source.[6] Albumin prepared by the same method inhibits the flocculation when derived from normal serum.[6,12] Albumin from a hepatitis patient does not inhibit flocculation as much as that

Dr. Tuft was formerly Medical Director of the Jewish National Home for Asthmatic Children, Denver, Colorado.

fraction from a normal patient.[12] Albumin itself from either source causes no flocculation.[12] Thus, the cephalin cholesterol flocculation test measures a balance between an inhibiting factor migrating with albumin and gamma globulin. Increase of the globulin alone can cause flocculation and decrease in the inhibiting factor while no increase in gamma globulin can produce the same result.[12]

Bauer,[13] using Cohn's technique, showed that the only fraction possessing inhibitory power was IV-7, which is a lipoprotein. The inhibiting factor was found only in the albumin fraction by Tiselius electrophoresis, but confirmation of this fact was not found by the paper method. Evidence points to an enzymatic type of action of the inhibitor, for aging normal sera even in the frozen state eventually results in flocculation in almost all samples.

Thymol turbidity and thymol flocculation are produced by a different mechanism.[14] Gamma globulin alone does not give increased turbidity nor positive flocculation. Lipids are quite important in the reaction, and apparently mediate changes in combination with both beta and gamma globulin. Up to 4.0 units is considered normal.[14] Flocculation occurs in sera containing a relatively high turbidity reading when the original test mixture is allowed to stand for eighteen hours.[11] No flocculation should occur in the normal patient.

Zinc turbidity and flocculation depend upon the ability of protein to form precipitates with this heavy metal in a buffered solution. Kunkel[3] stated that the gamma globulin obtained by Tiselius electrophoresis is the protein involved in the zinc sulphate test. Others[15] have stated that the correlation between gamma globulin and the turbidity test is not as good as originally proposed. Kunkel reported the normal range as between two and eight units. Other laboratories consider up to twelve units as within the normal limits.[16] For the purpose of this study, an upper limit of ten units was considered normal. Flocculation in this medium is again an extension of time that the components are allowed to remain in contact with each other. Very high gamma globulin levels in sera produce flocculation in a very few minutes. Normal sera do not flocculate for at least twelve hours. For purposes of this study, a time interval of two hours was selected for observing flocculation, since this correlates best with the range of turbidity units considered normal for this evaluation.

The entire panel of tests was applied to a total of 126 asthmatic patients, aged five to sixteen years, who were admitted to the Jewish National Home as intractable cases. One hundred twenty-one patients comprised the group for analysis of data on childhood asthma unmodified by steroid hormones. An additional five patients were tested only when on steroid medication, and, together with nine of the general group who were tested both on and off this drug, comprise the steroid-treated group.

A clinical classification of the untreated group, which considered only the time interval from the last asthmatic attack to the drawing of blood for the panel, was devised. This interval was arbitrarily set at within seven

days (Group A), eight to thirty-one days (Group B), and more than thirty-one days (Group C). The patients in Group A were the most chronic of the entire series. Those in Group B were having asthma only occasionally and their asthma was of the acute recurrent type. Those in Group C comprised the recovered patients, patients whose asthma had subsided upon admission to the Home and had not recurred.

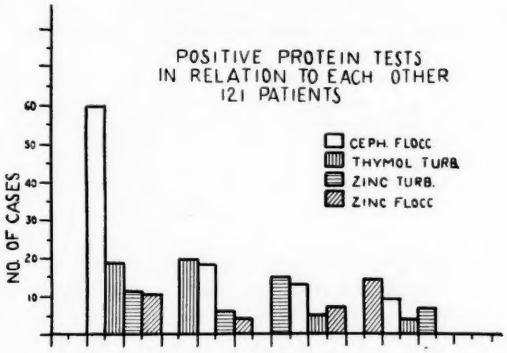


Fig. 1. Positive protein tests in relation to each other, in 121 patients.

RESULTS

Figure 1 shows the results of all the tests, except serum electrophoresis on paper, and the relationship of the tests to each other. The first bar in each group of bars represents the number of abnormalities for the test in question. Each of the other bars in the group represents the number of other test abnormalities found in the patients who manifested that abnormality. Abnormal cephalin flocculation tests occurred more frequently than all the other abnormal tests combined. Forty-nine per cent showed this abnormality, the majority reading two plus or higher. Increased thymol turbidity and zinc turbidity and positive zinc flocculation tests occurred with much less frequency. Results of thymol flocculation do not appear on this graph since no patient in the series showed this abnormality.

This figure also shows a marked discrepancy between the results of the various tests in relation to each other. For example, thymol turbidity was positive in only eighteen cases, zinc turbidity in only twelve, and zinc flocculation in eleven of the sixty patients who showed positive cephalin flocculation. There was a close relationship between increased thymol turbidity and cephalin flocculation and a similar situation existed in the case of zinc turbidity and cephalin flocculation. However, zinc turbidity and zinc flocculation showed little relation to increased thymol turbidity and to each other.

The increase in thymol turbidity was actually quite small, for of the

nineteen positive results, nine were in the borderline area of 4.1 to 5.0 units. The highest reading was 8.8 units, which is not significantly high when compared to the readings in hepatitis. Although one reading of 35 units was found, zinc turbidity increases were also generally of the borderline variety. On the other hand, the zinc flocculation positives were well marked with five one plus readings, two two plus, four three plus and the remainder, four plus.

TABLE I. RELATION OF PROTEIN TESTS TO CLINICAL CLASSIFICATION

Group	No. Cases	Cephalin Flocculation	Thymol Turbidity	Zinc Turbidity	Zinc Flocculation
A	44	21	6	7	4
B	38	20	10	4	4
C	39	19	3	4	6
S	14	4	1	0	0

Table I shows the data arranged for clinical classification as described above. Cephalin flocculation reactions occur in each group with approximately equal frequency. Distribution of positive reactions of the other tests through the clinical groups was also approximately the same except for thymol turbidity in Group B. No explanation for the increased percentage in this group is evident.

The influence of prednisolone on these abnormal protein tests is partially demonstrated by this chart. The incidence of cephalin flocculation reactions is lower in this group and only one of the other tests is positive. However, when cephalin flocculation was measured before, during and after a course of the drug, variation occurred, but the change was not consistent. Decrease in flocculation was noted during relatively short (less than two weeks) courses. Prolonged administration tended to cause return of the reaction to normal. In three patients, the reaction was markedly positive and remained so before and during a steroid course and thereafter. The one increased thymol turbidity test reaction occurred soon after the administration of the drug and returned to normal range while the drug was continued. Zinc turbidity and flocculation tests were unaffected by the drug.

Since significant hypergammaglobulinemia determined by paper electrophoresis was found to be characteristic of the asthmatic group and since increase in this fraction is known to be one of the mechanisms for the production of cephalin cholesterol flocculation, it was deemed worth while to examine the relationship of gamma globulin levels to cephalin cholesterol flocculation. All gamma globulin levels above 1.35 grams per cent, which was considered the top normal value, were plotted against the result of cephalin flocculation in each of these cases (Fig. 2). The top normal value used was an arbitrary one obtained by the addition of two times the standard deviation for the Durrum[17] paper electrophoresis method to the

actual top normal value obtained by this technique.[1] This chart demonstrated a lack of correlation between increased gamma globulin and cephalin flocculation inasmuch as there were a large number of elevated gamma globulin levels with negative tests. This was also demonstrated by

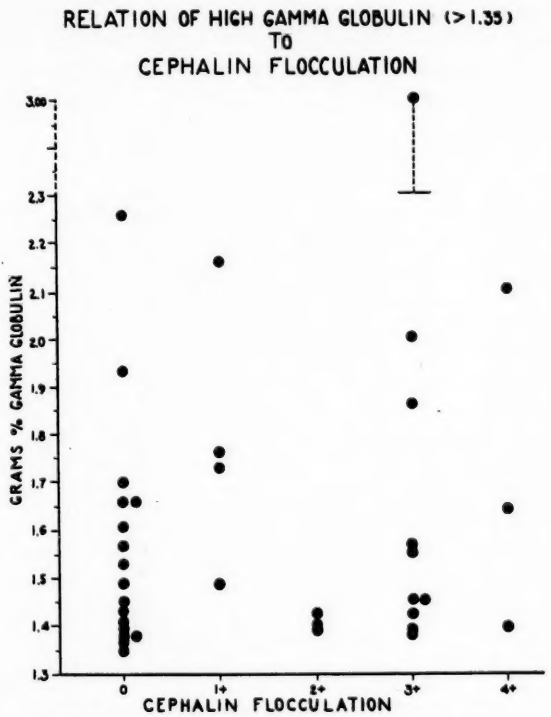


Fig. 2. Relation of high gamma globulin (>1:35) to cephalin flocculation.

plotting all of the positive cephalin flocculation reactions against gamma globulin levels (Fig. 3). A high percentage of the positive reactors demonstrated gamma globulin levels which fell within normal limits. These charts suggested that the absolute level of gamma globulin was not the critical factor in the production of cephalin flocculation in these patients, but that the so-called inhibitor factor was involved, either increased to counterbalance increased gamma globulin with no resultant flocculation or decreased with normal gamma globulin and resultant flocculation.

DISCUSSION

Certain practical considerations, as well as those of a more theoretical nature, are suggested by the data presented. First, the asthmatic child

showed serologic changes characteristic of disturbed liver function which do not appear to be related to significant liver disease. Therefore, tests for liver disease which are based on protein disturbances would have no diagnostic value in the asthmatic child, since these changes may well be

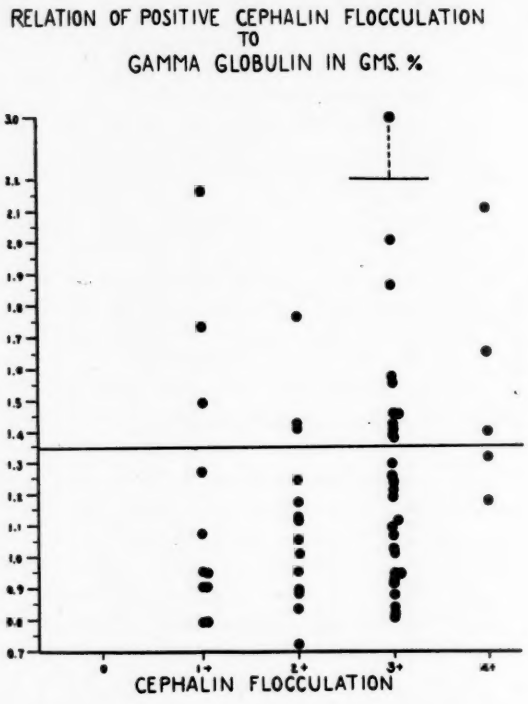


Fig. 3. Relation of positive cephalin flocculation to gamma globulin in grams per cent.

the result of asthma itself. Epidemics of hepatitis occur in children with some frequency. As a practical matter, it is important to interpret screening test data in an epidemic in the light of diseases other than hepatitis which may produce abnormalities.

The cephalin cholesterol flocculation test is especially worthless in a diagnostic situation of this type. Only a small percentage of the other liver function tests based on protein disturbances were positive in the asthmatic group, but the occasional positive may confuse the issue further in an individual case.

The cephalin flocculation reaction has been reputed to be "too sensitive." A theoretical explanation for its well-deserved reputation is suggested by the occurrence of significant positives in childhood asthma and the lack of

clinical or laboratory evidence of hepatic disease. Hypergammaglobulinemia was demonstrated in this group as a whole and this alone may cause flocculation in individual cases. However, the reaction may occur in the absence of elevation in gamma globulin and the so-called inhibitor factor may then be involved. It appears that cephalin cholesterol flocculation is the result of protein changes related to the immunology of certain diseases rather than to a specific hepatic cellular disease, although the data presented do not rule out the liver as the source of the changes. Further work on the identity and assay of the inhibitor is necessary to clarify this assumption.

SUMMARY AND CONCLUSIONS

1. Serologic protein changes usually characteristic of hepatic functional disturbance were found in a group of 121 asthmatic children. Sixty showed cephalin cholesterol flocculation, nineteen showed increased thymol turbidity, fifteen increased zinc turbidity and fourteen zinc flocculation. The abnormal protein tests were found to bear very little relation to each other. Because of this and the low incidence of all but the cephalin flocculation, the abnormalities were considered to have no relationship to significant hepatic cellular disease. Tests for hepatic cellular disease based on protein changes should be interpreted very carefully in the asthmatic child.

2. Cephalin flocculation reactions were found not correlative with increased gamma globulin levels. This variation in the so-called inhibitor substance was considered to be the important factor in the high number of positives discovered.

REFERENCES

1. Tuft, H. S.: Blood protein abnormalities in asthmatic children. J. Allergy, 27: 487-493 (Nov.) 1956.
2. Gray, S. J., and Guzman Barron, E. S.: J. Clin. Invest., 22:191, 1943.
3. Kunkel, H.: Estimation of alterations of serum gamma globulin by a turbidimetric technique. Proc. Soc. Exper. Biol. & Med., 66:217, 1947.
4. Kunkel, H. G., and Hoagland, C. L.: Mechanism and significance of thymol turbidity test for liver disease. J. Clin. Invest., 26:1060, 1947.
5. Gray, S. J.: The mechanism of the colloidal gold reaction of the blood in liver disease. Proc. Soc. Exper. Biol. & Med., 51:400, 1942.
6. Kabat, E. A.; Hanger, F. M.; Moore, D. H., and Landow, H.: The relation of cephalin flocculation and colloidal gold reactions to the serum proteins. J. Clin. Invest., 22:563, 1943.
7. Tuft, L.: Clinical Allergy. Second Edition. Philadelphia: Lea and Febiger, 1949, p. 343.
8. Urbach, E., and Gottlieb, P.: Allergy. New York: Grune and Stratton, 1946, p. 62.
9. Hanger, F. M.: The flocculation of cephalin cholesterol emulsions by pathological sera. Tr. A. Am. Physicians, 53:148, 1938.
10. MacLagan, N. F.: The thymol turbidity test as an indication of liver dysfunction. Brit. J. Exper. Path., 25:234, 1944.
11. Neefe, J. R., and Reinhold, J. G.: Laboratory aids in the diagnosis and management of infectious (epidemic) hepatitis. Gastroenterology, 7:393, 1946.
12. Moore, D. H., and Hanger, F. M.: Mechanism of the positive cephalin-cholesterol flocculation in hepatitis. J. Clin. Invest., 24:292, 1945.
13. Bauer, H. A.: Mechanism of modern serum tests in relation to their clinical significance. Rev. Gastroenteral., 6:158, 1949.

14. Recant, L.; Chargoff, E., and Hanger, F. M.: Comparison of the cephalin-cholesterol flocculation with the thymol turbidity test. Proc. Soc. Exper. Biol. & Med., 60:245-247, 1945.
15. De La Huerga, J., and Popper, H.: Estimation of gamma globulin and zinc turbidity tests with electrophoretic determination of gamma globulins. J. Lab. & Clin. Med., 35:466, 1950. Estimation of gamma globulin concentration by turbidemetry. J. Lab. & Clin. Med., 35:459, 1950.
16. Bowen, R.: Gamma globulin and the asthmatic child. Abst. in J. Allergy, 26:87, 1955.
17. Durrum, E. L., in Block, Durrum, and Zweig: A Manual of Paper Chromatography and Paper Electrophoresis. New York: Academic Press, Inc., 1955.

Submitted April 23, 1957
1635 East 18th Ave.

MANUSCRIPT EDITING SERVICE

For those physicians who are not familiar with the manuscript editing service, designed primarily for members of the American Medical Writers' Association, but offered to non-members at 50 per cent increase in the rates listed below, it was begun five years ago "to help authors say what they want to say." On the manuscript itself, punctuation, capitalization, spelling, misused words and arrangement of bibliography are corrected. In addition, the comments from the editor regarding title, organization, tables and illustrations, subheadings, summary, grammar, syntax and usage are given in a critical report.

The charges for this service based on the number of words in the manuscript are:

1000 words or less.....$5.00
Each additional 1000 words or fraction thereof.....$4.00

Manuscripts must be sent flat, via first class mail, typewritten in English, double or triple spaced, with wide margins, all sides. State the number of words in the manuscript in the upper right-hand corner of the first page and enclose the fee, plus return first class postage. The author should be sure to retain a carbon copy of his manuscript. Mail to: Harold Swanberg, M.D., 209-224 W.C.U. Bldg., Quincy, Illinois.

BILATERAL WHEEZING FROM AN ASPIRATED VEGETABLE (PEANUT?) FOREIGN BODY

A Case Report

AMPARO BUENAVENTURA, M.D., and LEON UNGER, M.D., F.A.C.A.
Chicago, Illinois

D. L., a three-year-old girl, was first seen by one of us (L. U.) on February 27, 1956, in his office because of "asthma" of five weeks' duration. She had been in a hospital for two weeks, but without relief. There was a rather vague history of so-called "asthma" on three different occasions, all within the past year. During one of these attacks the diagnosis of pneumonia was made. Birth and development were normal.

Examination revealed a slender child, in good condition, who weighed thirty pounds. The temperature was normal, but the pulse was 124 and the respiratory rate was thirty-two. The main findings were marked dyspnea and wheezing all over both lungs, about equal on the two sides. Fluoroscopic examination revealed some reduction in excursion of the diaphragm but was otherwise negative. The nasal mucosa was pale and glistening, and looked "allergic." The diagnosis of bronchial asthma seemed rather obvious.

Skin tests were carried out by the scratch method, supplemented by intradermals, but the tests were practically negative.

Epinephrine and potassium iodide were given but wheezing and dyspnea persisted. On March 3, the patient was sent to the pediatric ward of the Chicago Wesley Memorial Hospital, but even there the symptoms continued, along with a low fever (99-100.4 F.).

The erythrocytic sedimentation rate was 21 (slightly elevated); the hematocrit, 40; there was a leukocytosis of 23,250, with 55 per cent segmented neutrophils, 5 per cent unsegmented neutrophils, 34 per cent lymphocytes, 5 per cent monocytes, and 1 per cent eosinophils.

Achromycin was started (125 mg four times daily), but the pulmonary findings remained about the same, though there was some improvement for a few days. Elimination of eggs and citrus fruits did not help.

The symptoms by this time had lasted much too long for the diagnosis of bronchial asthma in a three-year-old girl. We began a search for other possible conditions. We ruled out mucoviscidosis, gamma globulin defects, and pressure from a double aortic arch.

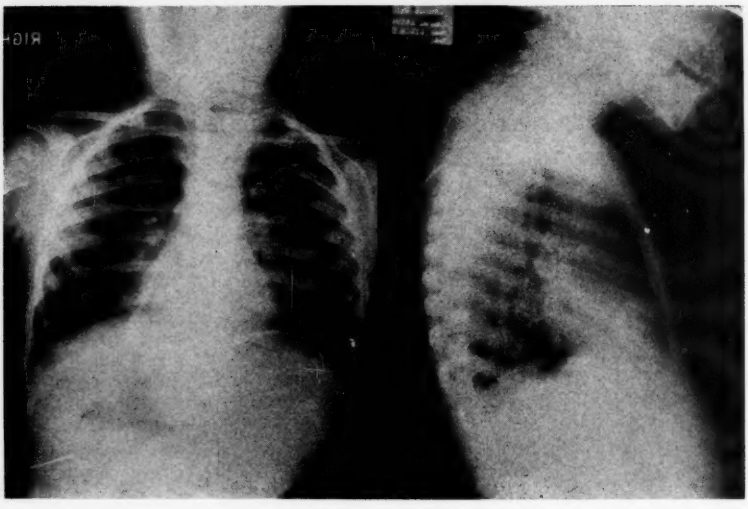
Roentgenograms were made repeatedly, but at first all were negative. On the eleventh hospital day, however, a film (Figs 1a and 7b) showed "a limited band of increased density in the right cardiophrenic angle which is believed to represent incompletely aerated lung presumably on the basis of bronchial plugging due to the asthma." On this day Tryptar inhalations were started, as follows: 25,000 units on the first day, 50,000 units on the second, and 75,000 units on the third day. Each inhalation was preceded by 0.10 cc 1:1000 epinephrine and 0.35 cc Histadyl subcutaneously. Wheezing continued but crepitant rales were

---

Presented at the Thirteenth Annual Congress of The American College of Allergists, Chicago, Illinois, March 21, 1957.

Dr. Buenaventura is Resident in Medicine, Chicago Wesley Memorial Hospital, 250 East Superior Street, Chicago, Illinois.

Dr. Unger is Attending Physician, Chicago Wesley Memorial Hospital, Chicago, Illinois, and Associate Professor, Department of Medicine, Northwestern University Medical School, Chicago, Illinois.



Figs. 1a and 1b.

now heard in the right lung field. On the seventeenth hospital day, fluoroscopy and chest films (Figs. 2 and 3) showed "normal heart; complete collapse of the right middle lobe, undoubtedly obstructive. This atelectasis is progressive and more marked than on 3-13-'56."

Bronchoscopy was carried out the next day and revealed abundant secretions, more on the right, but no real stenosis, although the bronchus to the right middle lobe appeared slightly narrowed. The bronchoscopist stated that the child was so small that good vision was not obtained. Accordingly, three days later a larger bronchoscope was inserted. A bolus of what appeared to be mucus was seen in the right primary bronchus, but only a small part of this could be removed.

During the procedure the anesthesia became light, and the child coughed something out. It appeared to be a peanut and biopsy showed it was of vegetable origin.

Recovery was dramatically prompt. The wheezing disappeared from both lungs, and three days later the child was asymptomatic and left the hospital. Since that time she has been seen by one of us (L. U.) at his office. The right middle lobe atelectasis disappeared within thirty-seven days. The child has remained free from wheezing these past twelve months. A chest x-ray taken three months after discharge (Figs. 4 (a) and 4 (b)) showed that the right middle lobe was normal and there was no infiltration in the lungs.

On further questioning of the family, it was found that peanuts were frequently eaten by the child's father and grandfather and were abundant in the home. We therefore believe that the vegetable foreign body expelled during bronchoscopy was almost certainly a peanut.

DISCUSSION

According to Jackson,[1,3] foods of vegetable origin are the most frequently encountered type of foreign body inhaled into the air passages. These vegetable materials provoke a violent reaction which is in marked

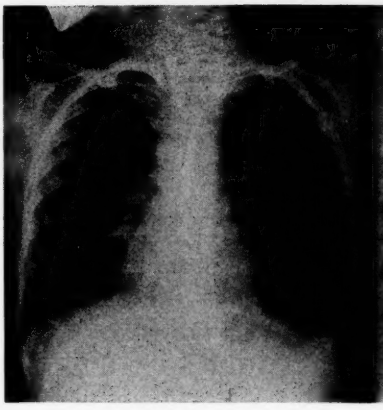


Fig. 2.

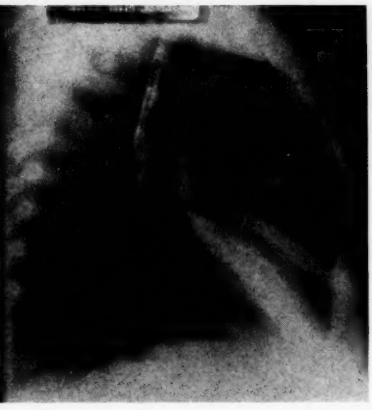
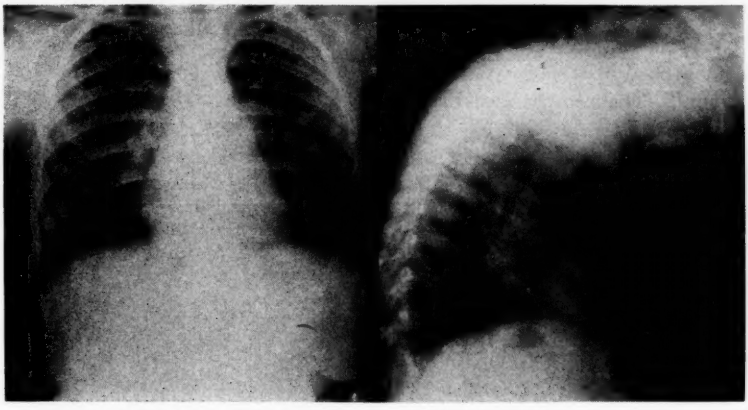


Fig. 3.



Figs. 4a and 4b.

contrast to the comparative absence of reaction from aspirated metallic objects. This irritating quality of vegetable matter may be chemical or allergenic in nature. A diffuse edema and inflammation of the tracheobronchial tree develops rapidly, within a few hours in a baby, and in a few days in an older child. The aspirated vegetable material may or may not produce complete obstruction, but soon, within a few days in a baby and in a week or two in older children, the mucosal swelling produces complete obstruction and atelectasis. All untreated cases are fatal, says Jackson, except in the rare instances when the foreign body is spontaneously expelled.

The term "vegetal bronchitis" was suggested by Jackson in 1925 to

describe the peculiar and septic tracheobronchitis associated with the aspiration of vegetable matter into the air passages. The condition is more frequent than is supposed because most of the cases are not diagnosed. Absence of a history of aspiration of a foreign body, the symptomless interval, and the diffuse physical findings are some of the reasons for errors in diagnosis.

Holinger[2] reported a case of a child four and a half years old in whom extensive mediastinal, pericardial, cervical and subcutaneous emphysema developing over a period of forty-eight hours led to the discovery of a peanut in the right bronchus. He emphasized that not infrequently in a child with "unresolved pneumonia" of unknown etiology, a vegetable foreign body, e.g., a peanut, can be found through a bronchoscope.

COMMENT

Our case demonstrates many of the peculiarities associated with aspiration of vegetable foreign bodies into the air passages. Wheezing was heard all over both lung fields, as is so commonly found in acute bronchial asthma. Jackson and his associates have pointed out that the mucosal reaction from vegetables is diffuse so that the physical signs are bilateral. They emphasized that a negative foreign body history is not important. X-ray evidence of obstructive emphysema or atelectasis is diagnostic. They recommended diagnostic bronchoscopy for all undiagnosed pulmonary disease. Without bronchoscopic examination and removal of the foreign body in our patient, the outcome would have been very doubtful.

Young children should not be given peanuts, peanut candy, nut candies or nut cakes; and children should not be allowed to play with peanuts, corn, peas, beans, coffee berries, and the like; all seeds should be removed from watermelons, oranges and grapefruit.

By contrast, foreign bodies of a metallic nature, when inhaled, can only cause unilateral wheezing unless the obstruction is high up in the respiratory tract. The diagnosis with these objects is much less difficult and an early roentgenogram is usually significant.

SUMMARY

1. A three-year-old child with a history and physical findings strongly suggestive of bronchial asthma, with bilateral wheezing, did not respond to usual therapy.

2. Roentgenograms were consistently negative at first, but finally showed evidence of atelectasis of the right middle lobe, presumably due to inhalation of a foreign body.

3. The foreign body, almost certainly a peanut, was removed at bronchoscopy, with dramatic and prompt improvement, and with re-expan-

sion of the collapsed lobe within thirty-seven days. There has been no recurrence of symptoms in the past year.

4. In young children, the dangers from inhalation of foreign bodies, especially peanuts, are emphasized.

REFERENCES

1. Jackson and Jackson: Bronchoesophagology. Philadelphia: W. B. Saunders, 1950.
2. Holinger, P. H., and Johnson, K. C.: Foreign bodies in the air and food passages. Pediatric Clin. North America, November, 1954.
3. Jackson, Chevalier: Overlooked cases of foreign bodies in the air and food passages. Brit. M. J., 2:686 (Oct. 17) 1925.

Submitted May 2, 1957

THE NEW ENGLAND SOCIETY OF ALLERGY

The annual meeting on Wednesday, March 19, 1958, Boston, Mass. All sessions will be held at Longwood Towers.

PROGRAM

Afternoon Session—2:00 p.m.

DR. JOHN L. FROMER, Presiding

"Identification and Counting of Pollen. Boston Pollen Surveys"—DR. RALPH WHEELER, Boston.

"Maine Pollen Surveys"—DR. MARTYN VICKERS, Bangor.

"Pollen Filters"—DR. FRANCIS CHAFEE, Providence.

"Specific Treatment of Pollinosis: Convention Therapy"—DR. J. EVARTS GREENE, Boston.

"Specific Treatment of Pollinosis: Abbreviated Therapy"—DR. FRANCIS M. RACKEMANN, Boston.

"Repository Treatment of Inhalant Allergy: Single Dose Therapy"—DR. MARY H. LOVELESS, New York.

Discussion

Social Hour—5:30 p.m.

Dinner—6:30 p.m.

Evening Session—7:30 p.m.

DR. FRANCIS M. RACKEMANN, Presiding

Business Meeting

1. Report of Nominating Committee.
   Dr. Lewis Webb Hill, Boston, for President
   Dr. Martyn Vickers, Bangor, Me., for Councillor (3 years)
   Other Nominations can be made by petition signed by 5 active members and sent to the Secretary at least 10 days prior to the Annual Meeting.
2. Election of Officers

"Management of Bronchial Asthma in Children"—DR. ROBERT CHOBOT, New York.

HISTORICAL DEVELOPMENT OF ALLERGY OF THE NERVOUS SYSTEM

FREDERIC SPEER, M.D., F.A.C.A.
Kansas City, Kansas

THERE is considerable evidence that the ancients were not far from a true understanding of the phenomena which we now class under the heading of nervous system allergy. Both philosopher and physician agreed that diet or digestion often had an unfavorable effect on the mind; the terms *hypochondria* and *melancholia* attest to this fact. When in the course of time more rational concepts made the humoral theory obsolete, the idea of food idiosyncrasy largely took its place, but the impression persisted that foods were in some way involved in the genesis of certain nervous disorders, especially headache and convulsions.

With the discovery of anaphylaxis and allergy, many observers were quick to see that here might be an answer to certain nervous diseases, and during the fifty years of the allergic era a number of these have been shown to be of allergic origin. It is the purpose of this paper to explore the development of this phase of allergy.

OBSERVATIONS PRECEDING THE DISCOVERY OF ALLERGY

Perhaps no work on nervous disease has been more widely read than Robert Burton's "The Anatomy of Melancholy."[1] This delightful collection of lore published in 1621 is the source of several pointed observations on diet and human behavior. In view of the fact that modern experience with food allergy has shown milk and legumes to be especially potent and common offenders, the following quotations from this seventeenth century source are truly remarkable. "Milk," said Burton, "and all that comes of milk, as butter and cheese, curds, &c. increase melancholy and are not good for those that have unclean stomacks, are subject to headache. . . ." And again, "All pulse are naught, beans, pease, fitches, &c.; they fill the brain (saith Isaac*) with gross fumes, breed black, thick blood, and cause troublesome dreams. And therefor which Pythagoras said to his scholars of old, may be for ever applied to melancholy men, eat no pease nor beans."

The literature of the eighteenth and nineteenth centuries has many references which reveal a continuing suspicion of the digestive tract in patients with nervous disorders. Much of this is concerned with faulty digestion and autointoxication, but in some cases specific foods were

---

From the Allergy Clinic, University of Kansas Medical Center, and the Allergy Clinic, Children's Mercy Hospital, Kansas City.

Presented at the Thirteenth Annual Congress of The American College of Allergists, Chicago, Illinois, March 22, 1957.

*Isaac Judaeus, Egyptian Jewish physician, tenth century, his works much studied at Salerno—Burton.

implicated. Fothergill[20] in 1778, speaking of his own migraine, reported that attacks invariably followed the eating of hot buttered toast for breakfast or the drinking of malted liquor which was "excessively hoppy." Willis,[60] writing in 1873, spoke of headaches due to "particular idiosyncrasies, from eating some special article of diet."

Convulsions, too, were early regarded as manifestations of food idiosyncrasy. In 1895, Fort[19] said, "We shall meet some cases who cannot eat certain articles of food without danger of spasm. For instance, I have under my care a child who has not had a spasm for more than a year, yet, if she should eat a teaspoonful of common beans, no matter how well cooked, it would, I am sure, precipitate one or more convulsions; in this case there seems to be a personal idiosyncrasy to this vegetable." He goes on to say, "There are some epileptics who cannot take milk in any form." And so again we encounter allergy to milk and legumes!

Fort's findings were confirmed in 1904 by Spratling,[51] who mentioned food idiosyncrasy as a cause of convulsions. He found strawberries, peaches, and shellfish of especial importance.

THE ALLERGIC ERA

With the discovery of anaphylaxis and allergy, a number of workers began to note the resemblance between anaphylactic shock and certain nervous phenomena. Since writers of the period were not greatly given to citing references, priority is not easily established, but the first such observations seem to have appeared in 1911. In that year, Shaw[48] reported a case of epilepsy as an anaphylactic reaction to egg and milk, and Herzfeld[26] reported that his own migraine was due to an anaphylactic reaction to foods. Within a decade or so, a considerable literature on neuroallergy had accumulated, and we may now consider the various manifestations under their appropriate headings.

Allergic Convulsions.—After the pioneer observations of Shaw, the first work done in allergic convulsions seems to be that of Pagniez and his associates[41] in 1919. Their interest lay mainly in showing the efficacy of peptone treatment. In 1921, Wechsler,[59] a neurologist, reported convulsions due to anaphylaxis, and in the following year, Ward[58] presented a large series of similar cases. These reports were followed in the next few years by those of Wallis[57] and Spangler[49] and many others, and it is clear from the large number of cases reported and the general tone of the articles that there was confidence that the answer to the age old riddle of epilepsy would be found at last in the field of allergy. When it began to appear that such a happy solution was not to be, interest dropped almost to the vanishing point, and as a result the possibility of an allergic origin is now generally neglected in the differential diagnosis of recurrent convulsions.

Allergic Headache.—In 1915, Rohrer[45] cited the case of a young physician whose migraine was of apparent anaphylactic origin. Two years later, Nast[38] reported anaphylactic migraine and experimented with peptone treatment. He continued this work in 1919 in association with Pagniez and Vallery-Radot.[40] Their writings seem to have attracted considerable attention, and were soon followed by the reports of Brown,[6] Vaughan,[54] and Miller and Raulston.[37]

Our present understanding of migraine as an allergic disease may be said to date from the well-documented paper of Vaughan,[55] which appeared in 1927. His findings were confirmed by Beecher,[5] Rowe,[46] Britten,[3] Rinkel,[4] Balyeat, [3,4] Ball,[2] and Goltman.[24,25] In 1931, Eyerman[18] greatly broadened our concept of cerebral allergy by showing that headache other than migraine is often due to allergy. Interest in recurrent headache has been further increased by the work of Ogden,[39] who has drawn attention to the importance of headache of inhalant origin. The importance of remembering that children, too, may have allergic migraine has been stressed by Glaser.[22]

Undoubtedly migraine and other recurrent cephalalgias are the most widely recognized manifestations of neuroallergy, and they are now given thorough consideration in all allergy texts. There is, in fact, considerable sentiment among allergists that migraine is primarily an allergic disease.[53]

Allergy and Behavior.—Early workers in anaphylaxis seem to have worked on the assumption that this strange new discovery might affect any system of the body. Hoobler, in 1916,[28] outlined the characteristics of allergic children and was careful to include nervous manifestations. He noted that these children were often irritable, fretful, and sleepless, and remarked that this disturbed behavior was commonly their chief complaint. Shannon,[47] in 1922, took up this thought and published his classic description of neuropathic manifestations in allergic children. He insisted that their pattern of behavior constituted a distinct allergic syndrome which was not dependent on other allergic manifestations.

The first observation that neural activity might be depressed as well as excited by allergy seems to have been made by May,[36] who in 1923 reported allergic somnolence. Kahn[31] recognized that "languidness and restlessness" and "spells of intense temper and fury" were common in childhood pollinosis. This clinical picture, which the present writer[50] has termed "the allergic tension-fatigue syndrome," has been described by Crowe,[11] Clarke,[8] and Randolph,[43] and has even been noted in infants by Clein.[9]

In 1930, Rowe[46] extended the idea of behavior disturbances to adults. He reported such varied symptoms as irritability, mental confusion, fatigue, and despondency. To these symptoms, Davison[13] added insomnia

and personality change and such speech disturbances as aphasia and stuttering. Excellent studies of similar cases have been contributed by Kaufman.[32] Alvarez[1] described a "nervous storm" in which food allergy led to acute anxiety and prostration. In the work of Randolph,[44] disturbances of this type are seen as the elements of a distinct clinical entity whose manifestations occur in predictable fashion according to definite laws.

Other Types of Neuroallergy.—Although most of the work done in neuroallergy deals with headache, convulsions, and disturbed behavior, allergy has also been shown to be of importance in many other nervous diseases. Pardee,[42] Mathieu,[35] Jenkins,[29] Kennedy,[34] and Vaughan and Hawke[56] have shown that angioedema is capable of causing almost any type of neurologic episode. Duke,[16] and later Criep,[10] have described allergic vertigo. Glauzman[23] and Kennedy[34] early suggested the possibility that allergy might be a cause of multiple sclerosis, and Jonez[30] and Ehrenthiel and his associates[17] found practical application of this suggestion. Kennedy and Williams[33] presented evidence that stammering is of possible allergic origin, and Hinnant and Halpin[27] reported food allergy as a cause of cyclic vomiting in children. A significant contribution in neuroallergy was the finding of Dees and Lowenbach[14] that abnormal encephalograms are a common finding in all sorts of allergic children.

FAILURE OF NEUROALLERGY TO RECEIVE FULL RECOGNITION

The student of neuroallergy, searching for references in the dusty journals of the early 1900's, cannot help wondering why these observations were not taken up, expanded, and given wide application. Perhaps there is no single answer. It has occurred to the writer that there are at least three explanations: (1) overenthusiasm, (2) the rise of the psychogenic concept of disease, and (3) the failure of skin tests for foods.

1. *Overenthusiasm.*—It is doubtful if any disease of undetermined etiology escaped the enthusiasm of the early workers in anaphylaxis and allergy. When it became apparent that they had "bitten off more than they could chew," a reaction set in from which the specialty has not yet recovered.

2. *The rise of the psychogenic theory.*—As we have seen, early physicians assumed that organic factors lay at the root of nervous and mental disturbances. When their theories failed to hold up, the work of the psychotherapists led to the application of the psychogenic theory of disease to all diseases which were otherwise unexplained. Again, neuroallergy was the victim of overenthusiasm, this time from a totally unexpected quarter. It is enlightening in this connection to quote from the writings of Freud:[21] "Psychoanalysis depends on psychology for the disposition

of a good half of its psychiatric responsibilities. But it would be a serious error to suppose that analysis advocates or supports a purely psychological view of mental disorders. It cannot fail to recognize that the other half of the psychiatric task has to concern itself with the influence of organic factors (mechanical, toxic, infectious) on the psychic apparatus."

3. *The failure of skin tests.*—While skin tests came along to give brilliant confirmation to the work of Blackley and other pioneers in inhalant allergy, they have largely failed in foods, the common source of neuroallergy. Fortunately, Rowe and others who have worked long and hard to systematize the clinical testing of foods have brought improvement in the diagnosis of food allergy with the promise of renewed interest and success in this field.

THE FUTURE OF NERVOUS SYSTEM ALLERGY

When we consider its bright beginnings and its subsequent decline, it would be rash to predict great things for neuroallergy in the near future. What will happen depends primarily on the allergist. If he thinks of himself as a hay fever and asthma doctor and turns his back on nervous people, nothing will happen. If, on the other hand, he recognizes that the allergic reaction knows no bounds of tissue or organ but may be found at work anywhere, including the sensitive nervous system, he will find himself in a position to bring relief to many sufferers from nervous afflictions. He will do well to pay heed to the words spoken by the neurologist, Foster Kennedy,[34] over thirty years ago: "The solution of many of the epilepsies, migraine, and other paroxysmal disorders including, I believe, many of the psychoses, are behind locked doors of which we pick at. These will one day be opened by the key of biochemistry."

REFERENCES

1. Alvarez, W. C.: Puzzling nervous storm due to allergy. Gastroenterology, 7:241, 1946.
2. Ball, F. E.: Migraine—its treatment with peptone and its familial relation to sensitization diseases. Am. J. M. Sc., 173:781, 1927.
3. Balyeat, R. M., and Britten, F. L.: Allergic migraine. Am. J. M. Sc., 180:212, 1930.
4. Balyeat, R. M., and Rinkel, H. J.: Allergic migraine in children. Am. J. Dis. Child., 42:1126, 1931.
5. Beecher, W. L.: Migraine or sick headache. Illinois M. J., 55:123, 1929.
6. Brown, T. R.: Role of diet in etiology and treatment of migraine and other types of headache. J.A.M.A., 77:1396, 1921.
7. Burton, R.: The Anatomy of Melancholy, 1621. Edited by Dell, F., and Jordan-Smith, P. New York: Tudor Publishing Co., 1955.
8. Clarke, T. W.: The relation of allergy to character problems in children: a survey. Psychiat. Quart., 24:21, 1950.
9. Clein, N. W.: Cow's milk allergy in infants. Ann. Allergy, 9:195, 1950.
10. Criep, L. H.: Allergic vertigo. Pennsylvania M. J., 43:258, 1949.
11. Crowe, W. R.: Cerebral allergic edema. J. Allergy, 13:173, 1942.
12. Davison, H.: Cerebral allergy. South. M. J., 42:712, 1949.
13. Davison, H.: Allergy of the nervous system. Quart. Rev. Allergy & Applied Immunol., 6:157, 1952.

14. Dees, S. C., and Lowenbach, H.: The electroencephalograms of allergic children. Ann. Allergy, 6:99, 1948.
15. Dees, S. C.: Neurologic allergy in childhood. Pediat. Clin., North America, 1:1017, 1954.
16. Duke, W. W.: Ménière's syndrome caused by allergy. J.A.M.A., 81:2179, 1923.
17. Ehrenthiel, O. F.; Schulman, M. H.; and Alexander, L.: The role of food allergy in multiple sclerosis. Neurology, 2:412, 1952.
18. Eyerman, C. H.: Allergic headache. J. Allergy, 2:106, 1931.
19. Fort, S. J.: Some non-medical suggestions in the therapeutics of epilepsy. J.A.M.A., 25:1127, 1895.
20. Fothergill, J.: Remarks on the sick-headache, 1778. In: Liveing, E.: On Megrim, Sick Headache and Some Allied Disorders. London: Churchill, 1873, p. 8.
21. Freud, S., quoted by Wortis, J.: Basic Problems in Psychiatry. New York: Grune and Stratton, 1953, p. 177.
22. Glaser, J.: Migraine in pediatric practice. Am. J. Dis. Child., 88:92, 1954.
23. Glauzman, E., in Hurst, E. W.: A review of some recent observations on demyelization. Brain, 67:103, 1944.
24. Goltman, A. M.: Unusual cases of migraine with special reference to treatment. J. Allergy, 4:51, 1932.
25. Goltman, A. M.: Mechanism of migraine. J. Allergy, 7:351, 1936.
26. Herzfeld, A.: Quinine in the preventive treatment of migraine and anaphylaxis. J.A.M.A., 57:1712, 1911.
27. Hinnant, I. M., and Halpin, L. J.: Food allergy in mild and severe cyclic vomiting. M. Clin. North America, 19:1931, 1936.
28. Hoobler, B. R.: Some early symptoms suggesting protein sensitization in infancy. Am. J. Dis. Child., 12:129, 1916.
29. Jenkins, C. M.: Cerebral edema due to phenobarbital sensitivity. Ann. Allergy, 7:346, 1949.
30. Jonez, H. D.: The allergic aspects of multiple sclerosis. California Med., 79:376, 1953.
31. Kahn, I. S.: Pollen toxemia. J.A.M.A., 88:241, 1927.
32. Kaufman, W.: Primary food-induced allergic syndromes and their secondary accompaniments. First International Congress of Allergists. Basel, Switzerland: S. Karger, 1952.
33. Kennedy, A. M., and Williams, D. A.: Association of stammering and the allergic diathesis. Brit. M. J., 2:1306, 1938.
34. Kennedy, F.: Allergic manifestations in the nervous system. New York State J. Med., 36:469, 1936.
35. Mathieu, E.: A case of deep urticaria complicated with paralysis of the brachial plexus. Union méd. du Canada, 61:377, 1932.
36. May, E.: Unnatural somnolence. Bull. et mém. Soc. méd. d. hôp. de Paris, 47:704, 1923.
37. Miller, J. L., and Raulston, B. D.: Treatment of migraine with peptone. Evidence of the anaphylactic character of the seizure. J.A.M.A., 80:1894, 1923.
38. Nast, A.: Treatment of migraine. C. R. du groupement medico-chirurgical de la Ve region, March 9, 1917, p. 155. Cited by Pagniez et al.[40]
39. Ogden, H. D.: Inhalant sensitization in allergic headache. South. M. J., 41:931, 1948.
40. Pagniez, P.; Vallery-Radot, P.; and Nast, A.: Essay on the preventive treatment of certain migraines. Presse méd., 27:173, 1919.
41. Pagniez, P., and Lieutaud, P.: Phenomena of the anaphylactic type in the pathogenesis of certain epileptic attacks. Presse méd., 27:693, 1919.
42. Pardee, I.: Two cases demonstrating allergic reactions in the central nervous system. J. Nerv. & Ment. Dis., 88:89, 1938.
43. Randolph, T. G.: Fatigue and weakness of allergic origin (allergic toxemia) to be differentiated from nervous fatigue and neurasthenia. Ann. Allergy, 3:419, 1945.
44. Randolph, T. G.: Allergy as a causative factor of fatigue irritability and behavior problems in children. J. Pediat., 31:560, 1947.
45. Rohrer, F.: Symptoms of anaphylaxis in migraine. Med. Klin., 11:876, 1915.
46. Rowe, A. H.: Allergic toxemia and migraine due to food allergy. California and Western Med., 33:785, 1930.
47. Shannon, W. R.: Neuropathic manifestations in infants and children as a result of anaphylactic reactions to foods contained in their dietary. Am. J. Dis. Child., 24:89, 1922.

48. Shaw, H. B.: Hypersensitiveness. Lancet, 2:713, 1911.
49. Spangler, R. H.: Allergy and epilepsy: analysis of 100 cases. J. Lab. & Clin. Med., 13:41, 1927.
50. Speer, F.: The allergic tension-fatigue syndrome. Pediat. Clin., North America, 1:1029, 1954.
51. Spratling, W. P.: Epilepsy and Treatment, Philadelphia: W. B. Saunders Co., 1904, p. 113.
52. Stevenson, L. D., and Alvord, E. C., Jr.: Allergy in the nervous system. Am. J. Med., 3:614, 1947.
53. Unger, A. H., and Unger, L., Migraine is an allergic disease. J. Allergy, 23:429, 1952.
54. Vaughan, W. T.: Diseases associated with protein sensitization. Virginia M. Monthly, 49:316, 1922.
55. Vaughan, W. T.: Allergic migraine. J.A.M.A., 88:1183, 1927.
56. Vaughan, W. T., and Hawke, I. K.: Angioneurotic edema with some unusual manifestations. J. Allergy, 2:125, 1931.
57. Wallis, R. L. M.; Nice, W. D.; and Craig, M.: The importance of protein hypersensitivity in the diagnosis and treatment of a special group of epileptics. Lancet, 1:741, 1923.
58. Ward, J. F.: Protein sensitization as a possible cause of epilepsy and cancer. New York M. J. & Record, 115:592, 1922.
59. Wechsler, I. S.: The treatment of epilepsy. M. Rec., 100:714, 1921.
60. Willis, S.: On sick headache. Brit. M. J., 1:8, 1872.
61. Winkelman, N. W., and Moore, M. T.: Allergy and nervous diseases. J. Nerv. & Ment. Dis., 93:726, 1941.

Submitted March 22, 1957
2601 Parallel Avenue

"His (the physician's) is the only profession in almost universal direct contact with the general public, and any thinking doctor will be aware that, if he has been qualified five years and has not been reading regularly, he is distinctly out of date. In my view, if he has been qualified ten years and has not read regularly, he is dangerously uninformed. The situation of anyone who left medical school twenty years ago and is still working on the teaching he received as a student without postgraduate education from journals, books, or meetings, is, unless he be a very unusual man, almost medieval as far as important parts of medical practice are concerned."—WILLIAM PHILLIPS, *The Disintegrative Action of the Nervous System* (The Lancet, CCLXXII:287, 1957)

* * *

The method of scientific investigation is nothing but the expression of the necessary mode of working of the human mind. It is simply the mode at which all phenomena are reasoned about, rendered precise and exact. There is no more difference, but there is just the same kind of difference, between the mental operations of a man of science and those of an ordinary person, as there is between the operations and methods of a baker or of a butcher weighing out his goods in common scales, and the operations of a chemist in performing a difficult and complex analysis by means of his balance and finely-graduated weights. It is not that the action of the scales in the one case, and the balance in the other, differ in the principles of their construction or manner of working; but the beam of one is set on an infinitely finer axis than the other, and of course turns by the addition of a much smaller weight.—T. H. HUXLEY—Darwiniana, 1863.

PRESIDENTIAL ADDRESS

ETHAN ALLAN BROWN, M.R.C.S. (Eng.), L.R.C.P. (Lond.)
Boston, Massachusetts

FOR almost fifty years the meanings of words have fascinated, puzzled, beguiled and bemused me. One word which has always been of particular interest to me, as it has been to many others, is the word "pleasure." It was my intent to thank you for the privilege and pleasure of serving you as your President. But so used, the word "pleasure" is indeed difficult to define.

The dictionary tells us that pleasure is a state of gratification of the senses or mind; an agreeable sensation or emotion; the excitement, relish or happiness produced by expectation or enjoyment of something good, delightful or satisfying; delight, enjoyment, joy. It states that opposed to pleasure are pain and sorrow. The word is defined further as sensuous gratification for its own sake; amusement, sport, diversion, self-indulgence and sensual gratification. Supposedly synonymous are the words satisfaction, happiness, cheerfulness, gaiety, mirth, merriment, jollity, hilarity, delight, delectation, gladness, joy and enjoyment. I mean none of these.

I once sat in on an unforgettable discussion between Sir Almroth Wright and his philosophical secretary, the Reverend Father Frederick Hastings Smyth, to both of whom I owe so much. The word pleasure was then being discussed for Sir Almroth Wright's book, "Prolegomina to Knowledge."

"Pleasure," said Sir Almroth, as best I can remember his words and I doubt that I will ever forget one of them, "could be defined in at least three frames of reference." There are first the immediate responses to external sights, sounds, tastes and smells. Beautiful scenery and good music are pleasant. We must all agree that these give us "pleasure." Such pleasure is close to the dictionary meaning of the word.

The second definition of the word "pleasure" applies to the "carnal" satisfactions of inner tensions craving relief. These concern empty organs which must be filled and full organs which must be emptied. Hunger, thirst and sex are such tensions, but physical fatigue and cold should also be included. There is no doubt that not only good food and drink, but that easy rest, deep sleep and warmth after cold are "pleasures." Here we have in part gone beyond the dictionary definition.

It is when we attempt to define pleasure in its third context that we get into difficulties. There is a special type of pleasure derived from activities often otherwise considered unpleasant. What makes this concept of pleasure complex and difficult to define, said Sir Almroth

Presented at The Thirteenth Annual Congress of The American College of Allergists, March 21, 1957, Chicago, Illinois.

Wright, "is that the same activities are truly ambivalent and, depending upon the circumstances, may be pleasant or unpleasant." Think of a school boy learning how to do percentages and the same boy working out a Big League batter's batting average! One of two soldiers in full equipment slogging through a swamp says, "Isn't this Hell?" In another part of the same swamp two hunters, equally equipped, say to each other, "This is the life!"

Further discussion privately and publicly of the meanings of the word pleasure led Sir Almroth Wright to state that it was an insult for someone who had done neither true physical nor truly creative mental work to say to one in the middle of the misery of such work that it was done because the worker found it a "pleasure." And apropos of his work, he also said that he prayed to God to forgive him for a day wasted when at bedtime he found himself neither mentally nor physically tired.

Then why did he or do we do the work we do and why, if we do it, does it either please us or make us happy?

The compelling desire to learn something, to understand something or to explain something lies deep within us. If one lacks this inner, as it were, "nuclear reactor," everything one does is hard work and certainly not a pleasure. If one does possess it, one would, if marooned on an island in the Pacific, take pleasure in classifying its flora and fauna as soon as the physical desires of hunger, thirst and shelter were satisfied.

We all know that in study itself there is never any end in sight! In research, the proportion of success to failure is infinitesimal and the road is slippery with the tears of your predecessors. The rewards are so slight, and so meager!

As Gladstone said of statesmanship, it can be said of research, that trying to discover where God Almighty is going during the next five years, and trying to run around in front of him is really the most difficult of all the jobs you can choose for yourself.

Well then, if we do what we want to do, and having done these things, accept as rewards square pieces of parchment, why does anyone seek these symbols of what may be called success? It is not for fame! From where I stand I can point out any number of College members who could easily acquire fame by sending to the journals some of their, as yet, unpublished work. Their desire to know, and not only to know but to understand in the Faustian sense, transcends their desire for fame.

I think that the answer must be the same as that given by the man who conquered Mount Everest. When asked why he climbed to its peak, he answered, "Because it is there." It was certainly no privilege. It was certainly no pleasure to climb Everest.

And I, too, feel that for most of us it is neither a pleasure nor a privilege to do the work we do. It is not done for fame, for fortune or,

for that matter, for the approval of our colleagues. In many cases may I say, the results are just the opposite!

We must work toward understanding the problems of allergy because the problems are there. If some of us are privileged to be executives of an organization of physicians and research workers engaged in such work, the honor is merely incidental. The problems are there. Some, if not most of us, must try to explain them away. When we have explained them away, the problems we now see will no longer be there. But previously hidden behind them new problems will become apparent. Some of us will have to explain those away. Invisible at present, but standing there all along, other problems will show themselves. These too, must be explained away. There will always be problems and there will always be those who will want explanations.

I am happy to follow in the immediate footsteps of Dr. Lawrence J. Halpin, who has been a good friend to me. I am equally happy to be followed by Dr. Orval R. Withers whose staunch friendship I have always enjoyed. I look further back to my good friends, Dr. Homer E. Prince, Dr. M. Murray Peshkin and Dr. Harold A. Abramson, and further forward to your nominee for President-Elect, my good friend, Dr. Merle A. Moore. I am proud to have stood in my place in this group.

"My dear René, I think great things are coming to pass. Joseph Meister has just left the laboratory. The three last inoculations have left some pink marks under the skin, gradually widening and not at all tender. There is some action, which is becoming more intense as we approach the final inoculation, which will take place on Thursday, July 16. The lad is very well this morning, and has slept well, though slightly restless; he has a good appetite and no feverishness. He had a slight hysterical attack yesterday."

The letter ended with an affectionate invitation. "Perhaps one of the great medical facts of the century is going to take place; you would regret not having seen it."—RENE VALLERY-RADOT: "Louis Pasteur and the Conquest of Rabies," from *The Life of Pasteur.*

POSSIBLE UNUSUAL OCCURRENCE OF HOMOLOGOUS SERUM HEPATITIS FOLLOWING PASSIVE TRANSFER STUDIES

Case Report

PAUL F. DEGARA, M.D., F.A.C.A.
Pelham Manor, New York

PASSIVE transfer studies have been employed by allergists since this reaction was first described in 1921 by Prausnitz and Küstner. However, in using this valuable method, one must be aware of the inherent danger of transmitting jaundice with infected serum. A case where this possibly occurred due to unusual circumstances will be presented.

A four and one-half-months-old, dark-colored infant was admitted to New York Hospital with eczema, since the age of three months, progressively increasing in severity. He also had profuse diarrhea and was dehydrated. The child had been under constant medical supervision since birth and at no time was jaundice noted. During his first two weeks at the hospital, he was given eight plasma injections, totalling 320 cc, and ten blood transfusions, totalling 315 cc; he also received albumin, antibiotics and steroids.

Approximately ten to twelve weeks later, when the infant was eight months old, serum was obtained for passive transfer studies, which were done on the patient's father, a thirty-three-year-old, colored elevator operator, native of the British West Indies, who had no personal history of allergy.

About nine weeks after being injected with his son's serum for Prausnitz-Küstner studies, the father developed fatigue and "chilly sensations." Subsequently, he became anorexic and nauseated with occasional vomiting in the morning. He noticed that his stools were clay-colored, and that his urine was dark. Finally, his sclerae became yellow.

Twelve weeks after the passive transfer studies, the father was admitted to New York Hospital with infectious hepatitis. There was no history of any surgical or parenteral procedure on him since the passive transfer studies were done. The father remained at the hospital for six weeks and was discharged in good condition. Significant laboratory data on admission included:

Urine: Bile ++
Blood: Bilirubin 18.7 mg
Thymol turbidity 15 units
Cephalin flocculation 4 units
Bromsulfaein retention 17.9%
Alkaline phosphatase 6.3 units

From the Pediatric Allergy Clinic, New York Hospital—Cornell Medical Center, New York City.
Presented at the Thirteenth Annual Congress of The American College of Allergists, Chicago, Illinois, March 22, 1957.

COMMENT

Viral hepatitis, its problems and progress to 1954 have been recently summarized by Neefe[1] of the University of Pennsylvania. It is known that human blood and feces are the only sources of hepatitis virus and that it may be present in very high concentrations, so that 50 cc of a 1:1,000,000 dilution of whole blood, or 0.0001 to 0.00001 cc, may be infectious. The finding of virus in blood or stools in the absence of clinical symptoms of hepatitis, and also the existence of long-term asymptomatic blood or feces carriers of the virus without a history of diagnosed hepatitis, have been reported.

There was no history of jaundice or hepatitis in the child in this report whose serum was used for passive transfer studies; however, nonicteric mild viral hepatitis is not uncommon in young children. The infant's father, likewise, had no history of jaundice, nor of other contacts that could explain the subsequent occurrence of hepatitis. It is noteworthy that the patient had received numerous transfusions with both human plasma and blood, two to three months before the passive transfer studies were done. The possibility that hepatitis virus was present in one of the blood or plasma specimens used for transfusion cannot be definitely excluded. No hepatic tests were done in the infant, because at that time no suspicion of viral hepatitis was entertained; also, these tests in young infants are not dependable.

DISCUSSION

Evidence that the father's hepatitis was due to the passive transfer studies performed with his son's serum is presumptive and not substantiated. Nevertheless, this case is of interest because it calls attention to a somewhat unusual possibility of transmitting homologous serum hepatitis.

It should be pointed out that persons who had blood transfusions within the past six months are not accepted as blood donors.[2] This precaution is recommended to avoid the risk of transmitting hepatitis virus that could have been present in the blood used for transfusion.

While the Prausnitz-Küstner test remains a most valuable and important tool in allergy studies, it must be borne in mind that serum from patients with a history of hepatitis within five years[3] or of blood transfusions within six months[2] preceding the planned passive transfer studies may be a source for transmitting homologous serum hepatitis.

SUMMARY

Serum from an eight-month-old dark-colored infant with atopic eczema was used for passive transfer studies on the patient's father. There was no history of jaundice in the patient who had been under constant medical observation since birth, but three months prior to the passive transfer studies the child had received numerous blood transfusions. Eighty-four

days after being injected with his child's serum, the father was admitted to the hospital with homologous serum hepatitis.

REFERENCES

1. Neefe, J. R.: Viral hepatitis. Am. J. Med., 16:710-728, 1954.
2. Kellner, A.: Personal communication.
3. Matthes, M. and Riderer, W.: Wie Lange Zeit sollen Blutspender nach einer Hepatitis von Blutentnahmen ausgeschlossen werden. Deutsch. Med. Wchschr., 81:1914-1917, 1956.

876 James Street
Submitted March 22, 1957.

THE ROLE OF RESEARCH

Research not only adds to our knowledge but also supplies an understanding and insight into the interrelationships of knowledge. Science formerly was a means of getting to know the world; now it is enlisted to change the world. It is a disservice to unify where no unity exists by trying to explain phenomena of different natures on a single basis. Hypothesis must not be confused with proof. Conflicting hypotheses and doctrines stimulate investigation to determine truth. Distraction from the primary purpose or objective of research often causes great inefficiency. The eye must be kept on the target. Even the most precise data are meaningless unless they are directly related to the phenomena under investigation.—Hoops, H. C.: On the philosophy of research, Texas Rep. Biol. & Med., 14:362-371, 1956.

HEALTHY?

Health is no longer viewed in the negative sense as the mere absence of disease. Health connotes a harmony of mind and body with self and environment. This balance will obtain with the normal activity of every vital and supporting function. The nice adjustments of the body to its surroundings have been grouped under the term homeostasis by Cannon. Selye has extended this concept in his theory of adaptation. The internal milieu of the mammalian body is a complex, ever-changing medium of physical, physiological, and chemical factors so integrated in health as to maintain a sense and a presence of well-being.—Middleton, William S.: The natural history of disease, J.A.M.A., 162:568 (Oct.) 1956.

Preliminary Program

GRADUATE INSTRUCTIONAL COURSE IN ALLERGY

April 20-22, 1958

and

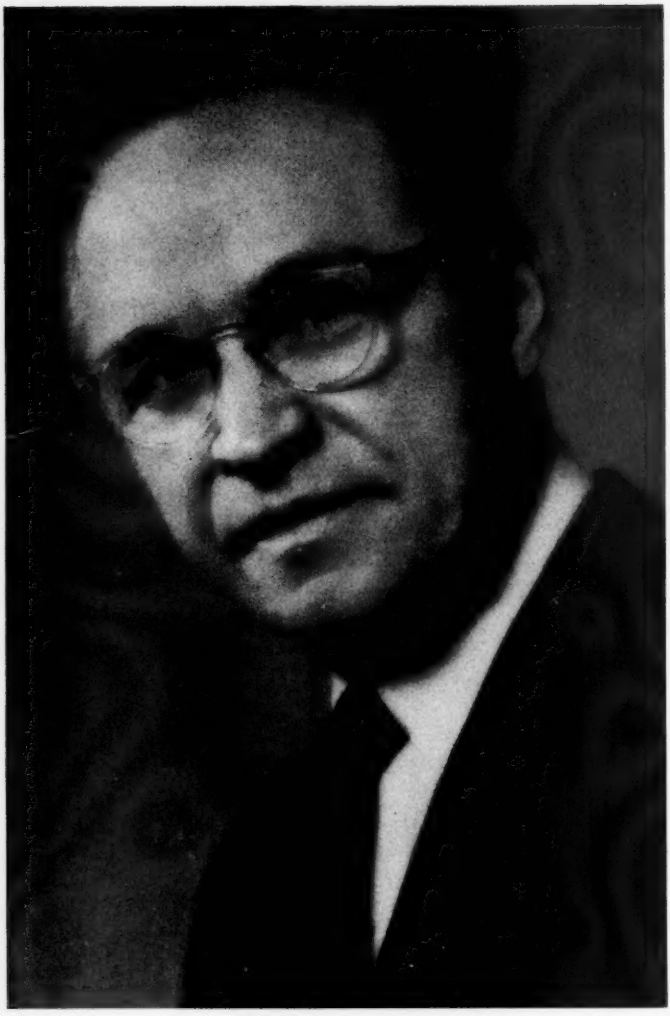
FOURTEENTH ANNUAL CONGRESS

The American College of Allergists

April 23-25, 1958

The Shelburne

Atlantic City, New Jersey



ORVAL R. WITHERS, M.D.
Kansas City, Missouri
President, 1957-1958

PRESENT OFFICERS

President—ORVAL R. WITHERS, M.D.
President-Elect—MERLE W. MOORE, M.D.
First Vice President—GILES A. KOELSCHE, M.D.
Second Vice President—HUGH A. KUHN, M.D.
Executive Vice President and Counsel—ELOI BAUERS
Secretary—DAVID R. THOMAS, M.D.
Treasurer—JOHN D. GILLASPIE, M.D.

BOARD OF DIRECTORS

Chairman—ETHAN ALLAN BROWN, M.R.C.S., England; L.R.C.P., London.
Vice Chairman—ORVAL R. WITHERS, M.D.
President-Elect—MERLE W. MOORE, M.D.
First Vice President—GILES A. KOELSCHE, M.D.
Member, Board of Regents—CECIL M. KOHN, M.D.

BOARD OF REGENTS

	Term Expires
KENNETH L. CRAFT, M.D., Indianapolis, Indiana	1960
PHILIP GOTTLIEB, M.D., Philadelphia, Pennsylvania	1958
MAYER A. GREEN, M.D., Pittsburgh, Pennsylvania	1960
GEORGE F. HIEBER, M.D., St. Petersburg, Florida	1960
S. H. JAROS, M.D., Harlingen, Texas	1958
CECIL M. KOHN, M.D., Kansas City, Missouri	1958
HOWARD G. RAPAPORT, M.D., New York, New York	1959
SAM H. SANDERS, M.D., Memphis, Tennessee	1959
W. C. SERVICE, M.D., Colorado Springs, Colorado	1959
ORVAL R. WITHERS, M.D., Kansas City, Missouri	

PROGRAM COMMITTEE

MERLE W. MOORE, M.D., Portland Oregon *(Over-all Chairman)*

HARRY L. ROGERS, M.D., and PHILIP M. GOTTLIEB, M.D., Philadelphia, Pennsylvania *(Co-Chairmen, Instructional Course)*

MAURICE C. BARNES, M.D., Waco, Texas *(Chairman, Dermatologic Allergy Session)*

EDLEY H. JONES, M.D., Vicksburg, Mississippi *(Chairman, Ophtho-Otolaryngologic Session)*

HOWARD A. RAPAPORT, M.D., New York, New York *(Chairman, Pediatric Allergy Session)*

BENNETT KRAFT, M.D., Indianapolis, Indiana *(Chairman, Psychosomatic Session)*

THERON G. RANDOLPH, M.D., Chicago, Illinois *(Chairman, Allergy of the Nervous System Session)*

STEPHEN D. LOCKEY, M.D., Lancaster, Pennsylvania *(Chairman, Technology Session)*

ETHAN ALLAN BROWN, M.R.C.S., England; L.R.C.P., London, Boston, Massachusetts *(Program Consultant)*

PRELIMINARY PROGRAM

Fourteenth Annual Postgraduate Course in Allergy

(Preliminary Program—subject to minor changes)

SATURDAY, APRIL 19, 1958

Afternoon Registration—Georgian Room

3:00—Registration at The Shelburne

SUNDAY, APRIL 20, 1958

Morning Session—Grande Ballroom

8:00—Registration

FUNDAMENTALS OF ALLERGY

Chairman: PHILIP M. GOTTLIEB, M.D., Philadelphia, Pennsylvania

Co-Chairman: SAM H. SANDERS, M.D., Memphis, Tennessee

9:00—Basic Mechanisms and Physiology of Allergic Diseases

HAROLD A. ABRAMSON, M.D., Associate Attending Physician for Allergy, The Mount Sinai Hospital; Assistant Clinical Professor of Physiology, Columbia University, New York, New York

9:45—Immunology

MERRILL W. CHASE, Ph.D., Associate Professor, Rockefeller Institute for Medical Research, Laboratory of Immunology, New York, New York

10:30—RECESS

10:40—Pathology of Allergic Diseases

GORDON R. HENNIGAR, JR., M.D., Professor of Pathology, State University of New York, College of Medicine; Pathologist-in-Chief and Associate Director of Laboratories, Kings County Hospital, Brooklyn, New York

11:25—The Release of Serotonin and Histamine During Anaphylaxis

T. PHILLIP WAALKES, M.D., PH.D., Senior Investigator, Clinical Section, General Medicine and Experimental Therapeutics, National Heart Institute, The National Institutes of Health, Bethesda, Maryland

Afternoon Session—Grande Ballroom

Chairman: SUSAN C. DEES, M.D., Durham, North Carolina

1:00—Skin Testing and the Diagnostic Approach to the Allergic Patient

LEON UNGER, M.D., Associate Professor, Department of Medicine, and Attending Physician, Allergy Clinic, Northwestern University Medical School, Chicago, Illinois

1:35—Patch Tests

MAX GROLNICK, M.D., Attending Allergist in Charge of Allergy Division, Jewish Hospital of Brooklyn; Clinical Associate Professor of Medicine (Allergy), State University College of Medicine, Brooklyn, New York

1:45—Pollen and Mold Identification

NATHAN SCHAFFER, M.D., Chief of Allergy, East Orange General Hospital and Orange Hospital Center, East Orange, New Jersey

2:25—The Study of the Eosinophile in the Diagnosis of the Allergic State

JAMES A. MANSMANN, M.D., Director of the Department of Allergy, Saint Francis General Hospital; Assistant Professor of Medicine, University of Pittsburgh School of Medicine, Pittsburgh, Pennsylvania

2:35—RECESS

THE ALLERGIC SYNDROMES

Chairman: M. MURRAY PESHKIN, M.D., New York, New York

2:45—PANEL on Nasal Allergy

The Rhinologist and Nasal Allergy
KARL M. HOUSER, M.D., Professor of Otolaryngology, University of Pennsylvania School of Medicine; Director of Otolaryngology, Children's Hospital of Philadelphia

L. DELL HENRY, M.D., Head of Department of Allergy, St. Joseph Mercy Hospital, Ann Arbor, Michigan; Consultant Allergist, Beyer Memorial Hospital, Ypsilanti, Michigan

Non-Seasonal Allergic Rhinitis and the Treatment of Nasal Allergy
GILES A. KOELSCHE, M.D., Assistant Professor of Medicine, Mayo Foundation, University of Minnesota; Consultant, Division of Medicine, Mayo Clinic, Rochester, Minnesota

SUNDAY, APRIL 20, 1958

OFFICE AND LABORATORY PROCEDURES

Mirror Room

4:00—How to Write Histories

JONATHAN FORMAN, M.D.
Worthington, Ohio

4:30—Methods of Testing

(Scratch, Intradermal, Insufflation, Ophthalmic, Patch)
Interpretation, Values, Fallacies. A Practical Demonstration
LEON UNGER, M.D.
Chicago, Illinois

5:00—Methods Employed in the Preparation of Highly Purified Dust, Mold and Pollen Extracts

STEPHEN D. LOCKEY, M.D.
Lancaster, Pennsylvania

PRELIMINARY PROGRAM

MONDAY, APRIL 21, 1958

Morning Session—Grande Ballroom

THE ALLERGIC SYNDROMES (Continued)

9:00—PANEL on Bronchial Asthma

Moderator: WILLIAM C. SERVICE, M.D., Colorado Springs, Colorado
Co-Moderator: DAVID R. THOMAS, M.D., Augusta, Georgia

Pulmonary Function Tests
ALLAN HURST, M.D., Assistant Clinical Professor of Medicine, University of Colorado School of Medicine; Attending Physician and Director, Inhalation Therapy Department, General Rose and St. Anthony's Hospitals, Denver, Colorado

The Use of Drugs in the Treatment of Bronchial Asthma
JOHN C. KRANTZ, JR., Ph.D., Professor of Pharmacology, School of Medicine, University of Maryland, Baltimore, Maryland

Environmental Control and Hyposensitization
MORRIS A. KAPLAN, M.D., Clinical Associate Professor of Medicine and Director, Allergy Research Unit, Department of Medicine, The Chicago Medical School; Director, Mount Sinai Medical Research Foundation, Chicago, Illinois

Intractable Asthma
HAROLD S. TUFT, M.D., Assistant Clinical Professor of Medicine, The University of Colorado School of Medicine, Denver, Colorado

10:30—RECESS

10:40—PANEL on Food and Gastro-intestinal Allergy

Moderator: ETHAN ALLAN BROWN, M.R.C.S., England; L.R.C.P., London, Boston, Massachusetts
Co-Moderator: HERMAN A. HEISE, M.D., Milwaukee, Wisconsin

Clinical Manifestations
MILTON MILLMAN, M.D., Consultant in Allergy, Paradise Valley Sanitarium and Hospital, San Diego, California

Diagnosis and Control of Food Allergy—I
THERON G. RANDOLPH, M.D., Staff Physician, Saint Francis Hospital, Evanston, Illinois

Diagnosis and Control of Food Allergy—II
ALBERT H. ROWE, M.D., Lecturer in Medicine, University of California Medical School, San Francisco; Allergist, Samuel Merritt Hospital, Oakland Naval Hospital, Oakland, California

Afternoon Session—Grande Ballroom

Chairman: JONATHAN FORMAN, Worthington, Ohio
Co-Chairman: GEORGE F. HIEBER, St. Petersburg, Florida

1:00—Recent Studies in Antibody Formation and Transfer
MERRILL W. CHASE, Ph.D., Associate Professor, Rockefeller Institute for Medical Research, Laboratory of Immunology, New York, New York

1:25—Drug Allergy
CARL F. SCHMIDT, M.D., Sc.D., Professor of Pharmacology, University of Pennsylvania School of Medicine, Philadelphia, Pennsylvania

1:50—Allergic Diseases of the Eyes

ALBERT D. RUEDEMANN, SR., M.D., Professor of Ophthalmology, Wayne State College of Medicine; Chief of Ophthalmology, Harper and Detroit Receiving Hospitals, Detroit, Michigan

2:10—Vascular Headache (including color and sound film)

HENRY D. OGDEN, M.D., Assistant Professor, Department of Medicine, Louisiana State University School of Medicine, New Orleans, Louisiana

2:30—Ménière's Syndrome

HUGH A. KUHN, M.D., President, Indiana Academy of Ophthalmology and Otolaryngology, Hammond, Indiana

2:40—RECESS

2:50—PANEL on Dermatologic Allergy

Infantile Dermatoses
SUSAN C. DEES, M.D., Associate Professor of Pediatrics and Allergy, The Duke University School of Medicine; Assistant Pediatrician, Duke University Hospital, Durham, North Carolina

Adult Dermatoses
ROBERT F. DICKEY, M.D., Department of Dermatology, The George F. Geisinger Memorial Hospital, Danville, Pennsylvania

Contact Dermatitis and Dermatitis Medicamentosa
JAMES M. FLOOD, M.D., Chief of Section on Dermatology, The Guthrie Clinic, Sayre, Pennsylvania; Associate in Dermatology and Syphilology, Graduate School of Medicine, University of Pennsylvania

Urticaria and Angio-Edema
JEROME GLASER, M.D., Assistant Professor of Pediatrics, University of Rochester School of Medicine and Dentistry; Pediatrician-in-Chief, Genesee Hospital, Rochester, New York

MONDAY, APRIL 21, 1958

OFFICE AND LABORATORY PROCEDURES

Mirror Room

4:00—The Threshold Test, Its Value as a Diagnostic and Therapeutic Adjunct

MARY H. LOVELESS, M.D., New York, New York

4:30—Causative Diagnosis in Contact Dermatitis

GEORGE L. WALDBOTT, M.D., Detroit, Michigan

5:00—Procedures of Value in Cold Filtration

STEPHEN D. LOCKEY, M.D., Lancaster, Pennsylvania

7:00—Informal Buffet Supper—Main Dining Room

(Tickets may be purchased separately at the Registration Desk until 2:00 P.M., Monday, April 21, 1958.)

The fee for the Instructional Course is $50 for non-members for three days, $35 for two days, and $20 for one day. *This fee includes the buffet supper Monday evening.* For all members of the College in good standing the fee for the entire course is $15, *which does not include the buffet supper.*

PRELIMINARY PROGRAM

TUESDAY, APRIL 22, 1958

Morning Session—Grande Ballroom

Chairman: MERLE W. MOORE, M.D., Portland, Oregon

Co-Chairman: SAMUEL E. RYNES, M.D., Philadelphia, Pennsylvania

ADVANCED CONCEPTS IN ALLERGY

9:00—Hormones
STANISLAUS H. JAROS, M.D., Consultant, Harlingen State Tuberculosis Hospital, Harlingen, Texas

9:20—New Principles of Antibody-Antigen Interaction as Applied to Allergy
VICTOR A. NAJJAR, M.D., Professor and Chairman, Department of Microbiology, Vanderbilt University School of Medicine, Nashville, Tennessee

9:50—Liver Disease and Antibody Formation
W. PAUL HAVENS, JR., M.D., Professor of Clinical Microbiology and Director, Division of Infectious Diseases, Department of Medicine, Jefferson Medical College, Philadelphia, Pennsylvania

10:10—The Auto-Immune Diseases in Hematology
MAX M. STRUMIA, M.D., Director of Laboratory, The Bryn Mawr Hospital, Bryn Mawr, Pennsylvania, Professor of Pathology, University of Pennsylvania Graduate School of Medicine

10:40—RECESS TO VISIT EXHIBITS

10:50—Bacterial Allergy
MURRAY DWORETZKY, M.D., Assistant Professor of Clinical Medicine and Assistant Professor of Clinical Public Health and Preventive Medicine, Cornell University Medical College, New York, New York

11:15—Essentials of Mold Allergy
HOMER E. PRINCE, M.D., Clinical Professor of Medicine, Baylor University College of Medicine, Houston, Texas; President, The Association of Allergists for Mycological Investigations, Inc.

11:45—Present-Day Aerosol Therapy
ROBERT T. CATHCART, M.D., Director, Cardio-Respiratory Laboratory, Jefferson Medical College Hospital, Philadelphia, Pennsylvania

Afternoon Session—Grande Ballroom

Chairman: HARRY L. ROGERS, M.D., Philadelphia, Pennsylvania

Co-Chairman: JOHN L. FOX, M.D., Upper Darby, Pennsylvania

1:00—Collagen Diseases: Some Relationships to Allergy
WILLIAM A. SODEMAN, M.D., Magee Professor of Medicine and Head of Department, Jefferson Medical College, Philadelphia, Pennsylvania

1:30—The Rare Allergic Syndromes
ORVAL R. WITHERS, M.D., Associate Clinical Professor of Medicine, University of Kansas Medical School; Head of Allergy Clinic, University of Kansas Medical Center, Kansas City, Missouri

1:50—Physical Allergy

CECIL M. KOHN, M.D., Chief of Allergy, Menorah Medical Center; Chief of Allergy, Kansas City General Hospital, Kansas City, Missouri

2:10—Insect Sting Allergy

BOEN SWINNY, M.D., Instructor in Allergy Clinic, University of Texas and Baylor University, San Antonio, Texas

2:30—RECESS

2:40—Obstructive Pulmonary Emphysema

ALLAN HURST, M.D., Assistant Clinical Professor of Medicine, University of Colorado School of Medicine; Attending Physician and Director, Inhalation Therapy Department, General Rose and St. Anthony's Hospitals, Denver, Colorado

3:00—Loeffler's Syndrome

HAROLD L. ISRAEL, M.D., Associate Professor of Medicine, Graduate School of Medicine, University of Pennsylvania; Chief, Department of Medicine, Philadelphia General Hospital, Philadelphia, Pennsylvania

3:20—Film: Stress and the Adaptation Syndrome (color and sound)

Prepared by NORMAN P. SCHENKER, M.D., and LEO L. LEVERIDGE, M.D., in collaboration with HANS SELYE, M.D. (Presented courtesy of the Pfizer Laboratories)

TUESDAY, APRIL 22, 1958

OFFICE AND LABORATORY PROCEDURES (Continued)

Mirror Room

4:00—ROUND TABLE DISCUSSION

Specific Hyposensitization Treatment; Methods of Preparing, Diluting and Administering Extracts

LEON UNGER, M.D., Chicago, Illinois; HOMER PRINCE, M.D., Houston, Texas; IRWIN W. BARRETT, M.D., Clarksdale, Mississippi; MAYER GREEN, M.D., Pittsburgh, Pennsylvania; *Tentative Members:* GEORGE F. HIEBER, M.D., St. Petersburg, Florida; JEROME GLASER, M.D., Rochester, New York

TECHNICAL AND SCIENTIFIC EXHIBITS AT THE SHELBURNE

The booths of our exhibitors are worthy of your time and interest. During the midmorning and midafternoon of April 22, 23 and 24, Tuesday, Wednesday and Thursday until 5:00 P.M., those attending the Graduate Instructional Course and Scientific Sessions will be invited by the chairmen to visit the booths at the times indicated on the program.

The representatives in charge of the individual exhibits will be pleased to receive any suggestions or comments. Many exhibitors are advertisers in the ANNALS and Sustaining Members of The American College of Allergists. Your visits to the booths are an extension of the appreciation that the College has for the exhibitors.

PRELIMINARY PROGRAM

Fourteenth Annual Congress

WEDNESDAY, APRIL 23, 1958

Morning Session—Grande Ballroom

GENERAL SCIENTIFIC SESSION

Chairman: LAWRENCE J. HALPIN, M.D., Cedar Rapids, Iowa

Co-Chairman: R. DALE DICKSON, M.D., Topeka, Kansas

9:00—Current Concepts in the Treatment of Bronchial Asthma

ETHAN ALLAN BROWN, M.R.C.S., England; L.R.C.P., London. Boston, Massachusetts

9:30—A Study of the Effectiveness of Sustained-Action Tablets

S. WILLIAM SIMON, M.D., Chief, Allergy Clinic, Brown General Hospital, Veterans Administration Center, Dayton, Ohio; Assistant Professor of Medicine (Allergy), Ohio State University School of Medicine, Columbus, Ohio

10:00—RECESS TO VISIT EXHIBITS

10:15—Fluid and Electrolyte Therapy in the Management of Asthma in Infancy and Childhood

JOHN P. MCGOVERN, M.D., Clinical Associate Professor of Pediatrics, Microbiology and Allergy, Baylor Medical School and Texas University Post-Graduate School of Medicine, Houston, Texas

10:45—Some Recent Developments in the Mechanisms of Allergic Reactions

OSCAR SWINEFORD, JR., M.D.,* Professor, Internal Medicine, University of Virginia School of Medicine, Charlottesville, Virginia

11:15—RECESS TO VISIT EXHIBITS

11:30—The Possible Influence of Serotonin in Allergic Disease

M. COLEMAN HARRIS, M.D., Chief, Allergy Department, San Francisco Polyclinic and Post Graduate College, San Francisco, California, and NORMAN SHURE, Los Angeles, California

12:00—Influence of Pollenation on Blocking Antibody Output as Judged by Ophthalmic Tests

MARY H. LOVELESS, M.D., Associate Professor of Clinical Medicine, Cornell University Medical College; and CHARLES BLANDER, B.S., and THOMAS NALL, A.B., New York, New York

PRELIMINARY PROGRAM

Afternoon Session—Grande Ballroom

Chairman: GILES A. KOELSCHE, M.D., Rochester, Minnesota

Co-Chairman: GEORGE F. HIEBER, M.D., St. Petersburg, Florida

2:00—A Study of the Role of Released Substances, Such as Histamine, in the Mechanism of Anaphylaxis, Utilizing a Modified Schultz-Dale Technique

MURRAY DWORETZKY, M.D., Assistant Professor of Clinical Medicine, Cornell University Medical College, New York, New York

2:30—Pulmonary Denervation and Resection in Asthmatics

RICHARD H. OVERHOLT, M.D.,* Clinical Professor of Surgery, Tufts College School of Medicine; Director, Overholt Thoracic Clinic, Boston, Massachusetts

*By Invitation

3:00—RECESS TO VISIT EXHIBITS

3:15—Reactions to Influenza Vaccine

HERSCHEL E. GRIFFIN, LT. COLONEL, M.C.,* Chief, Communicable Disease Branch, Office of the Surgeon General, Department of the Army

3:45—Critical Analysis of the Properedin-Titration with Zymosan and C'3

MORRIS A. KAPLAN, M.D., Clinical Associate Professor of Medicine and Director, Allergy Research Unit, Chicago Medical School; and LUIGI LAMANTIA, M.D., Research Fellow in Allergy; and HOWARD LEE, B.S., Chicago, Illinois

4:15—RECESS TO VISIT EXHIBITS

4:30—Combined Steroid-Antibiotic Therapy in Allergies Associated with Infection

WILLIAM C. GRATER, M.D., Clinical Instructor in Medicine, Southwestern Medical School, Dallas, Texas

*By Invitation

PRELIMINARY PROGRAM

THURSDAY, APRIL 24, 1958

Morning Session—Grande Ballroom

GENERAL SCIENTIFIC SECTION

Chairman: CECIL M. KOHN, M.D., Kansas City, Missouri

Co-Chairman: JOHN MITCHELL, M.D., Columbus, Ohio

9:00—Use of a Tranquilizing Agent (Hydroxyzine) with Prednisolone in the Control of Allergic Disorders
JOHN L. FOX, M.D., Upper Darby, Pennsylvania, Clinical Assistant at Jefferson Hospital Allergy Clinic and Instructor in Allergic Diseases, Jefferson Medical College, Philadelphia, Pennsylvania

9:20—The Effect of Wind, Weather, and Populated Areas on the Distribution of Pollens and Molds (A Motion Picture)
HERMAN A. HEISE, M.D., and EUGENIA R. HEISE, M.T., Milwaukee, Wisconsin

9:40—The Treatment of Major Allergic Manifestations with Parabromdylamine Maleate Injectable (Dimetane)
J. WARRICK THOMAS, M.D., Assistant Professor of Medicine, Medical College of Virginia, Richmond, Virginia

10:00—RECESS TO VISIT EXHIBITS

PAPERS OF ASSOCIATE FELLOWS

10:15—Cough as an Allergic Symptom
SEYMOUR KAPLAN, M.D., Great Neck, L. I., New York

10:30—Hydroxyzine (Atarax) in Allergic Diseases
INES MARIA H. SANTOS, M.D., and LEON UNGER, M.D., Chicago, Illinois

10:45—A Study of the Nasal Cytology in Infants with Eczematoid Dermatitis
LLOYD CRAWFORD, M.D., Memphis, Tennessee

11:00—Delayed Reactions in Otolaryngology
A. R. MILLER, M.D., Seattle, Washington

11:15—RECESS TO VISIT EXHIBITS

11:30—The Treatment of Bronchial Asthma with Methylprednisolone (Medrol)
E. G. WYGANT, M.D., Chicago Heights, Illinois

11:45—Allergy Related to Bronchiectasis in Children
ARTHUR LIPSCHUTZ, M.D., Philadelphia, Pennsylvania

12:00—Patch Testing with Pollen Leaf Oleoresins
WARREN J. RAYMER, M.D., Houston, Texas

PRELIMINARY PROGRAM

THURSDAY, APRIL 24, 1958

Afternoon Session—Grande Ballroom

Chairman: ETHAN ALLAN BROWN, M.R.C.S., England; L.R.C.P., London
Boston, Massachusetts

2:00—The Nature of Allergy
WILLIAM E. SHERMAN, M.D.,* President, American Academy of Allergy; New York, New York

2:30—Distribution and Immunochemical Properties of Human Tissues and Tumor Antigens

Guest Speaker

LEONHARD KORNGOLD, PH.D.,* Section of Immunology, Memorial Center, New York, New York

3:30—Bela Schick and Von Pirquet Awards

4:15—Presidential Address
ORVAL R. WITHERS, M.D., Kansas City, Missouri
Introduction of MERLE W. MOORE, M.D., President-Elect; Portland, Oregon
Regular Business Meeting

6:30—Cocktail Party—The Solarium (Courtesy, The Schering Corporation)

8:00—Dinner Dance—Grand Ballroom (Wine, Courtesy Nepera Laboratories)

---

*By Invitation

PRELIMINARY PROGRAM

FRIDAY, APRIL 25, 1958

Morning Session—Mirror Room

ALLERGY OF THE NERVOUS SYSTEM

Chairman: THERON G. RANDOLPH, M.D., Chicago, Illinois

Co-Chairman: FREDERIC SPEER, M.D., Kansas City, Kansas

9:00—Allergic Fatigue and Toxemia
ALBERT H. ROWE, M.D., Oakland, California

9:35—Allergy of the Periphery Nervous System—A Review of Foster Kennedy's Contributions
DONALD S. MITCHELL, M.D., Montreal, P.Q., Canada

10:00—Vascular Headache (A Motion Picture)
HENRY D. OGDEN, M.D., New Orleans, Louisiana

10:30—RECESS

10:45—Sensory Phenomenon of Brain Allergy
THERON G. RANDOLPH, M.D., Chicago, Illinois

11:15—Alkali Therapy in Advanced Allergy
HARRY G. CLARK, M.D., Birmingham, Michigan

11:45—BUSINESS MEETING

FRIDAY, APRIL 25, 1958

Morning Session—Grande Ballroom

TECHNOLOGY

Chairman: STEPHEN D. LOCKEY, M.D., Lancaster, Pennsylvania

9:00—The Value of the Coombs Test for the Detection of Incomplete Antibodies in the Circulating Blood
A New Simple Sensitive and Reliable Method for the Serological Diagnosis of Infectious Mononucleosis
GEORG F. SPRINGER, M.D.* Assistant Professor of Immunology in Medicine and Microbiology, University of Pennsylvania, Philadelphia

9:30—Technology of Repository Immunization in Allergic Disorders
MARY H. LOVELESS, M.D., Associate Professor of Clinical Medicine, Cornell University Medical College, New York, New York

9:50—A Simple Method of Cold Filtration
STEPHEN D. LOCKEY, M.D., Chief, Department of Allergy, Lancaster General Hospital, Lancaster, Pennsylvania
or
SIDNEY ROSEN, Ph.D.,* Engineer, National Instrument Company, Baltimore, Maryland

10:00—RECESS

10:10—DEMONSTRATION: Vital Capacity and Maximum Breathing Capacity
(Actual apparatus and audience participation)
RICHARD T. CATHCART, M.D.* Assistant Professor of Medicine, Director of Cardio-Respiratory Laboratory, Jefferson Medical College, Philadelphia, Pennsylvania

11:00—Thrombocytopenic States, Immunological Aspects

HAROLD A. WURZEL, M.D.* Assistant Professor of Clinical Pathology and Medicine, School of Medicine, University of Pennsylvania, Philadelphia, Pennsylvania

11:40—Some Technological Aspects of Preparing Allergenic Extracts

JOHN A. SCIGLIANO, Ph.D.* Chief, Pharmaceutical Development Service, National Institutes of Health, Bethesda, Maryland

*By Invitation

FRIDAY, APRIL 25, 1958

Morning Session—Brady Room

PEDIATRIC ALLERGY

Chairman: HOWARD G. RAPAPORT, M.D., New York, New York
Co-Chairman: NORMAN W. CLEIN, M.D., Seattle, Washington

8:00—BREAKFAST, Courtesy of The Borden Company, New York

9:00—The Effect of Steroids and Antihistamines on Scratch Testing

SIDNEY APPEL, M.D.,* ARTHUR A. GOLDFARB, M.D., and VICTOR SZANTON, M.D. Children's Allergy Clinic, Bronx Municipal Hospital, Bronx, New York

9:15—Rice Intolerance in Infants: Masked Food Allergy?

DOUGLAS E. JOHNSTONE, M.D., Department of Pediatrics, University of Rochester School of Medicine and Dentistry, Rochester, New York

9:30—Significance of the Components of Milk and Their Relationship to the Allergic Child

JOSEPH H. FRIES, M.D., Brooklyn, New York

9:45—Ulcerative Colitis in Known Allergic Patients

ETHEL M. DAVIS, M.D., Director, Children's Allergy Clinic, Cook County Children's Hospital, Chicago, Illinois

10:00—The Incidence and Significance of Urticaria and Angio-Edema in Children

M. MURRAY PESHKIN, M.D., New York, New York

10:20—COFFEE BREAK, Courtesy of The Borden Company, New York

10:45—Serous Otitis Media, Allergic Aspects in Childhood

HAROLD I. LECKS, M.D., Philadelphia, Pennsylvania

11:00—A Study of Allergy to Eggwhite

RICHARD L. LONDON, M.D.,* and JEROME GLASER, M.D., Rochester, New York

11:15—Cellular Aspects of Antibody Production

ALBERT H. COONS, Ph.D.* Professor of Bacteriology and Immunology, Harvard Medical School, Boston, Massachusetts

12:15—LUNCHEON—Main Dining Room

Subject: How Big Is an Antibody Combining Site?
Guest Speaker: ELVIN A. KABAT, Ph.D.,* Professor of Microbiology, Columbia University, New York

*By Invitation

PRELIMINARY PROGRAM

FRIDAY, APRIL 25, 1958

Afternoon Session—Grande Ballroom

DERMATOLOGIC ALLERGY

Chairman: MAURICE C. BARNES, M.D., Waco, Texas

Co-Chairman: OTIS FIELD JILLSON, M.D., Hanover, New Hampshire

2:00—Contributions of Dermatology to Allergy
SAMUEL J. ZAKON, M.D.,* Associate Professor of Dermatology, Northwestern University Medical School, Chicago, Illinois

2:30—Pitfalls in Diagnosis of Contact Dermatitis
OTIS FIELD JILLSON, M.D., Hitchcock Clinic, Hanover, New Hampshire

3:00—Nummular Eczema with Special Reference to Dermatitis of Housewives
PAUL GROSS, M.D.,* Clinical Professor of Dermatology, College of Physicians and Surgeons, Columbia University, New York, New York

3:30—The Problem of Cutaneous Vasculitis
BEATRICE MAHER KESTEN, M.D.,* Assistant Professor of Clinical Dermatology, College of Physicians and Surgeons, Columbia University, New York, New York
and
JOHN T. MCCARTHY, M.D.,* College of Physicians and Surgeons, Columbia University, New York, New York

4:00—Allergic Procaine Epidermal Hypersensitivity and Some Aspects of the Cross Sensitivity Pattern
ALEXANDER A. FISHER, M.D.,* Assistant Clinical Professor, Dermatology and Syphilology, New York University, New York

4:30—Contact Dermatitis Due to Ragweed and Other Pollen Oleoresins; Hyposensitization
JOHN L. FROMER, M.D., Lahey Clinic, Boston, Massachusetts

*By Invitation

FRIDAY, APRIL 25, 1958

Afternoon Session—Brady Room

OPHTHO-OTOLARYNGOLOGY

Chairman: EDLEY H. JONES, M.D., Vicksburg, Mississippi

Co-Chairman: FREDERICK H. THEODORE, M.D., New York, New York

2:00—Otolaryngologic Allergic Problems in Australia
HUGH A. KUHN, M.D., Hammond, Indiana

2:30—A Treatment of Nasal Polyposis
WALTER E. OWEN, M.D., Peoria, Illinois

3:00—A Kodachrome Clinic of Ocular Allergy
H. B. STAUFFER, M.D.,* Jefferson City, Missouri

3:30—Allergic Manifestations of the Larynx
BERNARD M. BARRETT, M.D.,* Pensacola, Florida

4:00—Allergic Manifestations in Otologic Disease
BEN H. SENTURIA, M.D.,* St. Louis, Missouri

*By Invitation

PRELIMINARY PROGRAM

FRIDAY, APRIL 25, 1958

Afternoon Session—Mirror Room

PSYCHOSOMATIC MEDICINE

Chairman: BENNETT KRAFT, M.D., Indianapolis, Indiana

Co-Chairman: MILTON J. STEINHARDT, M.D., Detroit, Michigan

2:00—Psychosomatic Group Therapy with the Parents of Children with Intractable Asthma

M. MURRAY PESHKIN, M.D., Chief Medical Consultant, and HAROLD A. ABRAMSON, M.D., Chief Research Consultant, New York, New York. The Jewish National Home for Asthmatic Children, Denver, Colorado

2:30—Symposium on Psychosomatic Medicine

HYMAN MILLER, M.D., Beverly Hills, California
JOHN H. MITCHELL, M.D., Columbus, Ohio
MILTON J. STEINHARDT, M.D., Detroit, Michigan

3:20—RECESS

3:30—Suicide by Asthma

BENNETT KRAFT, M.D., FRANK W. COUNTRYMAN, M.D., and DAVID BLUMENTHAL, M.S.W., Indianapolis, Indiana

3:50—Pseudo-Allergic Schizophrenia, A New Clinical Entity

HAROLD A. ABRAMSON, M.D., New York, New York
A five-minute discussion period will follow each paper

FRIDAY, APRIL 25, 1958

Evening Session—Mirror Room

7:00—A Workshop on Medical Writing

Chairman: JONATHAN FORMAN, M.D., Worthington, Ohio

INTRODUCTION—

DR. FORMAN

THE OBJECTIVES OF THE ANNALS OF ALLERGY—

ETHAN ALLAN BROWN, M.R.C.S., England; L.R.C.P., London, Boston, Massachusetts; Editor of ANNALS OF ALLERGY

PLANNING A PAPER

COMMUNICATION OF SCIENTIFIC FACTS

ERRORS IN WRITING

SUMMARY

PRELIMINARY PROGRAM

Instructional Course on Mold Allergy

Presented by
The Association of Allergists for Mycological Investigations, Inc.
The Shelburne, Atlantic City, New Jersey

FRIDAY, APRIL 25, 1958

Evening Session—Brady Room

7:00 p.m.—Registration
SIM HULSEY, M.D.

7:30 p.m.—Orientation
HOMER E. PRINCE, M.D.

7:40 p.m.—History of Mold Allergy
ETHAN ALLAN BROWN, M.R.C.S., England, L.R.C.P., London

8:00 p.m.—MOLD OCCURRENCES AND DISTRIBUTION, SYMPOSIUM
General and Geographic
NATHAN SCHAFFER, M.D.
Seasonal Variations
LAWRENCE J. HALPIN, M.D.
Environmental
E. P. LOWE, Ph.D.

9:00 p.m.—Mold Avoidance
D. J. PARSONS, M.D.

SATURDAY, APRIL 26, 1958

Morning Session—Brady Room

8:00 a.m.—LABORATORY INSTRUCTION
MARIE B. MORROW, Ph.D.
GEORGE H. MEYER, M.A.

10:30 a.m.—GEOGRAPHIC ASPECTS OF MOLD ALLERGY, PANEL
Moderator: BOEN SWINNY, M.D.
Scientific Advisor: MARIE B. MORROW, Ph.D.

Northeast
SAMUEL D. BELL, M.D.
North Central
DELL HENRY, M.D.
Pacific Northwest
LOIS FRAYSER, M.D.
Pacific Southwest
A. M. TARGOW, M.D.
South Central
DICK H. HUFF, M.D.
Southeast
JACK O. W. RASH, M.D.

11:40 a.m.—What Molds Will I Need and Where Will I Get Them?
GRACE TALBOTT, M.D.

12:00 noon—Testing with Mold Extracts
RITA DON, M.D.

12:30 p.m.—LUNCHEON—Mirror Room

1:30 p.m.—Treatment with Mold Extracts
HOMER E. PRINCE, M.D.

2:10 p.m.—QUESTION AND ANSWER PERIOD
Moderator: S. H. JAROS, M.D.
(All Instructors Participating)

A registration fee of $25 will be charged for this course. Preregistration is suggested, as enrollment will be limited. Address applications to The Association of Allergists for Mycological Investigations, Inc., Homer E. Prince, M.D., President, 808 Caroline Street, Houston 2, Texas.

PRELIMINARY PROGRAM

The Women's Auxiliary

The Solarium at The Shelburne will serve as the headquarters and Hospitality Room. Here Auxiliary members, wives of College members and their guests may relax in comfortable surroundings with playing cards and tables provided. The Solarium will be open from Sunday, April 20, at 2:00 p.m. until the close of the Congress on Friday, April 25.

TUESDAY, APRIL 22

2:00 P.M. Visit to Renault's Winery (transportation: $1.00 per person)

WEDNESDAY, APRIL 23

10:00 A.M. Fourth Annual Business Meeting of the Women's Auxiliary, The Solarium

12:00 Noon Annual Luncheon, Brady Room ($5.00 per person)
Guest of Honor: Ethan Allan Brown, M.R.C.S. (England); L.R.C.P. (London) Past President of The American College of Allergists

4:00 P.M. Exhibit of Contemporary Paintings, with Lecturer and Tea, The Solarium

THURSDAY, APRIL 24

11:00 A.M. Visit to Lenox China Showroom and Fischer Greenhouses (transportation: $1.50 per person)

3:30 P.M. The Presentation of the Auxiliary Bela Shick and Clemen von Pirquet Awards, Grande Ballroom, The Shelburne

6:30 P.M. Cocktail Party (Courtesy, The Schering Corporation)

7:30 P.M. Dinner Dance, Grande Ballroom

FRIDAY, APRIL 25

10:00 A.M. Coffee and cakes for College members and their wives, The Solarium

---

WOMEN'S AUXILIARY SCHOLARSHIPS

The Women's Auxiliary of The American College of Allergists announces that it has contributed to the College the sum of $300 for scholarships to the Instructional Course of the Fourteenth Annual Congress of the ACA, April 20-22, 1958, at Atlantic City, New Jersey. These scholarships will be awarded in accordance with the order in which applications are received and on the basis of the merit of the application. Physicians who wish to be considered for these scholarships should send their applications to the Program Chairman, Dr. Merle W. Moore, Medical Arts Building, Portland, Oregon.

TECHNICAL EXHIBITS

Booth		
33	Allergy-Free Products for the Home	Brooklyn, N. Y.
41	Allergy Laboratories, Inc.	Oklahoma City, Okla.
30	Almay Division, Schieffelin & Co.	New York, N. Y.
19	Ar-Ex Products Co.	Chicago, Illinois
18	Ayerst Laboratories	New York, N. Y.
10	Borden's	New York, N. Y.
42	Brewer & Company, Inc.	Worcester, Mass.
26	Center Laboratories, Inc.	Port Washington, N. Y.
17	Ciba Pharmaceutical Products, Inc.	Summit, New Jersey
7	The Coca-Cola Company	Atlanta, Georgia
32	F. A. Davis Company	Philadelphia, Pa.
39	Desitin Chemical Co.	Providence, R. I.
5	The DeVilbiss Company	Somerset, Pa.
1	Doho Chemical Corporation	New York, N. Y.
12	Dome Chemicals, Inc.	New York, N. Y.
3	Duke Laboratories, Inc.	South Norwalk, Conn.
23	Eisele & Company	Nashville, Tenn.
27	Encyclopaedia Britannica	Chicago, Illinois
22	Hugh Graham, Inc.	Dallas, Texas
9	Hollister-Stier Laboratories	Philadelphia, Pa.
2	Jackson-Mitchell Pharmaceuticals, Inc.	Culver City, Calif.
13	Knoll Pharmaceutical Company	Orange, New Jersey
31	Eli Lilly and Company	Indianapolis, Ind.
20	Loma Linda Food Company	Arlington, California
25	Marcelle Cosmetics, Inc.	Chicago, Illinois
8	Merck, Sharp & Dohme	Philadelphia, Pa.
16	C. V. Mosby Company	St. Louis, Mo.
29	Nepera Laboratories	Morris Plains, N. J.
36	Organon, Inc.	Orange, New Jersey
34	Parke, Davis & Company	Detroit, Mich.
43-44	Philco Corporation	Philadelphia, Pa.
14	Ralston Purina Company	St. Louis, Mo.
4	A. H. Robins Company, Inc.	Richmond, Va.
37	Sandoz Pharmaceuticals	Hanover, N. J.
28	Schering Corporation	Bloomfield, N. J.
24	G. D. Searle & Co.	Chicago, Illinois
46	Sharp & Sharp	Everett, Wash.
40	Stemen Laboratories, Inc.	Oklahoma City, Okla.
21	Stiefel Laboratories, Inc.	Oak Hill, New York
35	Testkit Laboratory	New York, N. Y.
6	Travenol Laboratories, Inc.	Morton Grove, Ill.
15	The Upjohn Company	Kalamazoo, Mich.
38	Westwood Pharmaceuticals	Buffalo, N. Y.
11	Winthrop Laboratories	New York, N. Y.

Progress in Allergy

DERMATOLOGIC ALLERGY

Critique and Review of the Recent Literature

JOHN L. FROMER, M.D., F.A.C.A.

Boston, Massachusetts

AN OVERWHELMING selection of material in the literature by American and foreign contributors is available for the reviewer of dermatologic allergy. A certain amount of selectivity must, therefore, be practiced in any compilation. Practicality and teaching value of the selections have been stressed. Undoubtedly, many valuable contributions have been omitted.

There is a trend toward earlier recognition and better management of light sensitive dermatoses. The problems of the group of allergic vasculitis are coming to be better defined. Newer knowledge is now available of delayed reactions to simple chemicals by intradermal testing. Single reports of drug allergy make up the highest proportion of contributions in this field. These reports are of particular value to the individual physician suddenly confronted with a distressing drug reaction and anxiously looking for a precedent for successful management.*

The review is divided for convenience into the following subsections: (1) allergic eczematous contact dermatitis; (2) atopic dermatitis; (3) urticaria and angioedema; (4) drug allergy; (5) steroid hormones, and (6) miscellaneous allergies.

ALLERGIC ECZEMATOUS CONTACT DERMATITIS

Experimental Studies.—As part of a Ciba seminar on recent advances in hypersensitivity, Chase[39] discussed the mechanism of sensitization in the guinea pig as it relates to drugs. The work of Dienes with protein sensitization showed that the first stage was a transient induction of a delayed type sensitivity. This event may be overshadowed almost immediately by the appearance of circulating antibodies and immediate type sensitivity. The work of Landsteiner and Jacobs in sensitization of animals with simple chemical compounds and the more recent work of Eisen, who concluded that different kinds of reaction products can occur between skin and the eliciting agents, depending upon the chemical properties of the entire structure, are mentioned. The role of heredity in drug sensitization of guinea pigs is also discussed. The transference of bacterial hypersensitivity in animals as well as the role of the lymphocyte and plasma cell in antibody production is briefly recorded. Lawrence[126] continued his studies in human beings of skin sensitivity of the tuberculin type with components of disrupted leukocytes. He found that the treatment of leukocyte components with the enzymes de-

From the Department of Allergy and Dermatology, The Lahey Clinic, Boston, Massachusetts.

*An abridgment of this review will be published in *Review of Allergy and Applied Immunology.*

soxyribonuclease (DNase) and ribonuclease (RNase) did not diminish the capacity to transfer delayed sensitivity. Eisen[61] stated that allergic contact dermatitis has all the essential characteristics of the delayed allergic response to tuberculin, both immunologically and histologically. He examined the sensitizing and eliciting properties of 2, 4-dinitro substituted benzene rings having, in labile position 1, a variety of reactive substituents (fluorine, chlorine, bromine, SO_3, SCl, SCN) and has employed chemical allergens marked with radiocarbon or radiosulfur for purposes of tracing *in vivo*. By this technique it was concluded that different kinds of reaction products can occur between skin and the antigenic agent, depending upon the chemical properties of the entire structure.[40]

Burrage and others[28] review medical progress in allergy. In a consideration of basic studies it was noted that not all of the properties of antigens are fully understood. Most antigens consist in part of protein, but certain polysaccharides and lipoids in combination with carbohydrates can produce antibodies in mammals. Haptens were developed by Landsteiner by combining diazo-salts with proteins. The important properties of antigens include the size of the chemical groups, their spatial arrangement, optical activity, number of amino acids and carboxyl groups at the end of the chain. There are several theories of antibody formation, the first being that antibodies are globulins and that their antibody properties are due to adaptation of their shape to that of the determinant group of the antigen. Antigen is necessary for antibody formation. Others believe that antigen must be present only to start antibody formation and that antibody formation may be prolonged after the disappearance of antigen. This theory would depend on the development of known properties of antibody formation in daughter cells. The sites of antibody production are still in dispute. Most living cells possess the ability to produce protein and therefore can theoretically produce antibody. Much work has centered around the lymphocyte and plasma cell. It has been shown that gamma globulin is a constituent of lymphocytes and that adrenocortical hormones dissolve lymphocytes, with the release of gamma globulin antibody. The red pulp of rabbit spleens when exposed to antigen contains large amounts of antibodies, whereas the follicular tissue, said to be mostly lymphocytes, produced few antibodies. Other investigators, using fluorescent antigens, added evidence favoring the plasma cell as the producer of antibody.

Waalkes and others[237] studied the release of serotonin and histamine during anaphylaxis in the rabbit. It had been known that histamine was released during anaphylaxis both *in vitro* and *in vivo*. Recent work has shown that serotonin is also released when antibody and antigen are added to normal rabbit platelets suspended in plasma. It is thought that during anaphylaxis serotonin is released from platelets while histamine is released from platelets and tissues. Spanoudis and others[218] were able to inhibit the local Shwartzman reaction by oral doses of dicumarol in sufficient dosage to lower the prothrombin time level below 1 per cent. Careful platelet counts were made in the rabbits given dicumarol as well as in the controls. It was found that the sensitizing injection produced a similar decrease of platelets as measured at twenty-four hours and a pronounced diminution fifteen to thirty minutes after the provoking injection. Both heparin and dicumarol have an inhibiting effect on the local Shwartzman reaction.

The Lancet[158] comments editorially on the origin of antibodies, stating that no one organ in the body produces antibodies to the exclusion of

all others. Antibodies are formed in the lymph nodes draining an area, and the kind of cell causing antibody synthesis is not known. The main site of antibody formation may be the plasma cells or their forerunners. Antibody production can be enhanced by the addition of adjuvants to the antigen. The effects of the adjuvant are ascribed partly to the delayed absorption of the antigen and prolongation of the stimulus in the lymph nodes and partly to the production of a local granuloma in which plasma cells are likely to develop. Transfer experiments with lymphatic and splenic tissue showed that antibody formation could be inhibited by respiratory and tissue poisons as well as by cortisone. Certain experiments indicate that although antibodies are produced in certain cells of lymph nodes and spleen, these cells may continue to produce antibodies after they are removed from their original host and transplanted into another animal or suspended in a culture medium outside the body.

Rostenberg[193] reviewed what is known about the production of eczematous reactions by allergic means and its distinction from eczematous reactions due to primary irritants. The pathologic alterations in primary irritant eczematous reactions and in allergic reactions are discussed. It is believed that eczematous persons are more vulnerable to mild primary irritants. It has been known that preliminary painting of the skin of guinea pigs with croton oil favored the development of a sensitization to picric acid in these animals. Freezing the skin with carbon dioxide prevented the development of an eczematous sensitization. It is concluded that the two types of eczematous reactions are intimately related but that there are important differences between them.

Frey and Wenk[76] isolated an island of skin on the guinea pig except for a narrow stem containing blood vessels and nerves. They found that no sensitization of either the island or the skin in general develops when dinitrochlorobenzene is applied to the island only. If the lymphatic vessels leading to the regional lymph node are preserved, sensitization does develop. It appears that the sensitizing substance must reach the lymph node and that generalization of sensitivity is carried through the blood stream.

Clinical Aspects.—Klauder[116] discussed some aspects of occupational dermatoses. Pitfalls in diagnosis, patch tests, prognosis, period of disability and period of recovery are especially stressed. Over 5,000 cases of cutaneous disease were reviewed and it was found that in 43.8 per cent of these the dermatoses were occupational in origin. Primary irritants caused 27.7 per cent of cutaneous disease; trauma and accidental injury 22.1 per cent, and sensitizing substances 15.2 per cent. The author believes that nonspecific polyvalent sensitization accounts for the continuation of occupational eczematous dermatitis after cessation of exposure. These features are often overlooked by the physician. Cross sensitization is discussed in compounds with a quinoline ring, nickel and cobalt, compounds with a quinone structure, which include paraphenylenediamine, sulfonamides, azo dyes, picric acid, and other aromatic nitro compounds, as well as certain local anesthetics and derivatives of paraaminobenzoic acid, frequently found in sunburn preventives. Schwartz[205] discussed occupational dermatitis in a special article in the *Quarterly Review of Allergy*. While this is a brief article, a useful table is appended of some important chemicals causing allergic occupational dermatitis, with recommended concentrations for patch testing.

Some of the most important contributions in current research are the observations on contact dermatitis due to nickel and chromate, with observations on dermal-delayed (tuberculin-type) sensitivity by Stephan Epstein.[63] He studied patients with contact dermatitis due to nickel and chromate. While these patients gave positive patch tests as was to be expected, it was also found that most patients had a delayed tuberculin-type response to 0.02 to 0.05 cc of a 1:40,000 dilution of nickel sulfate. Forty-two per cent of these patients also had a positive reaction to copper and 3 of 31 nickel-sensitive patients reacted to potassium dichromate. Five of 11 patients reacted to cobalt. All but 2 of the chrome-sensitive patients had positive reactions to both patch and intradermal tests. Following histologic studies, it was assumed that the evidence indicated that eczematous and tuberculin-type sensitivities were immunologically identical except for the site of the shock organ. Therefore, the concept of localized sensitivity must be re-evaluated. For example, it is known clinically that dermatitis from nickel-containing garters may occur only on one leg. Nickel contact dermatitis is usually papular or papulovesicular rather than bullous. Prurigo-like papules or lichenified lesions may be seen. Metastatic eczema or dermatitis may occur at distant sites or the eruption may spread for some distance beyond the area of direct contact with the metal sensitizer. Of 34 patients with nickel reactions, 10 showed signs of atopic dermatitis as well. This may also explain why chromate dermatitis in railroad workers, for example, may persist long after contact with all chromates has been eliminated. These studies may also be forerunners of attempts to desensitize patients with simple chemical dermatitis to graded injections with the same antigen in high dilution. While the recognition of dermal delayed sensitivity in contact dermatitis is of more theoretical than practical interest, it helps to explain why patients can be successfully "desensitized" to ragweed eczematous eruptions due to contact with the oily fraction of ragweed pollen, leaves or stems.

Calnan and Wells[31] reported nickel sensitivity in patients who wear stocking garters, earrings, brassiere clips or wrist watch bands in which the sensitivity appears at the initial site of contact. They outlined secondary sites that may be more important as eczematous problems than the primary eruption. The mechanism of the spread of sensitivity is not known. Sensitization from the thighs may spread to elbow flexures, eyelids, side of the neck and other portions of the extremities, and the eruption may even become generalized. The primary lesions are scattered papules and papulovesicles accompanied by erythema. Itching is more common in the secondary sites than in primary zones. Patch tests with nickel sulfate or nickel chloride in aqueous 1 to 2.5 per cent concentration are usually positive. It is important to remember that about 10 per cent of these patients may have a delayed reaction (up to ninety-six hours). Usually, response to therapy in patients with secondary nickel eruptions is slower.

Over a five year period, 198 patients who had nickel dermatitis were studied by Fisher and Shapiro.[71] These patients invariably reacted to patch tests with 10 per cent nickel sulfate solution. Patch testing with 2 per cent cobaltous sulfate did not reveal a high percentage of cross reactivity, which had been reported previously. Furthermore, 2 patients who were sensitive to cobalt were tested with 10 per cent nickel sulfate solution and neither was sensitive to nickel. Five per cent nickel sulfate was preferred to more concentrated solutions for patch tests. Patch tests

with nickel coins are reliable if the coins actually contain nickel. This metal was replaced temporarily with silver and manganese during World War II. Four of 40 patients lost their reaction to nickel over a period of years. Follow-up studies on the persistence or loss of sensitivity to contact agents are exceedingly important. Morgan reported the loss of this sensitivity in 43 per cent of a group of patients after periods of from one and a half to eleven years. Nielsen and Bang found that only 18 per cent of their patients lost their sensitivity to nickel after periods of from fourteen to nineteen years. In the series reported by Fisher and Shapiro, 10 per cent of the patients apparently lost their sensitivity to nickel over a period of from two to seventeen years. When the nickel coin is used for patch testing, nonspecific pressure effects must be avoided and papular, pustular reactions must not be confused with true allergic eczematous reactions. Sometimes follicular, miliaria-like reactions to nickel coins are seen. The true allergic eczematous reaction to the nickel coin is invariably accompanied by itching, erythema, papules and small vesicles.

Sams[199] observed 290 patients with contact photodermatitis over a period of twenty years. Lime oil has been established as a cause for dermatitis with photosensitization in a large series of patients. In 43 patients observed during the period the agent involved was either perfume or toilet water which had been applied to the area of the skin involved before exposure to sunlight. Sams, who practices in Miami, noted that contact photodermatitis is observed with increasing frequency. An additional number of patients had a dermatitis which is usually not localized but involves more diffusely the exposed surfaces; it is characterized by an erythematous eruption with papular and papulo-urticarial lesions. The eczematous component seldom shows gross vesiculation. It was thought that this group of patients were allergic to sun-screening agents. Patch tests with Skolex and neo-a-fil cream were done on a 5 year old girl. A positive reaction occurred when these agents were exposed to an erythema dose of ultraviolet light. There was no reaction without the use of the ultraviolet light. Sams found that a popularly used agent of digalloyl trioleate in 3.5 per cent alcoholic solution was capable of producing photodermatitis. This agent is widely used in sunscreen preparations. It is important to distinguish between phototoxic or photodynamic reactions and photoallergic reactions.

In an interesting report on dermatology in tropical and rural Cuba, Pardo-Castello[160] showed that eczematous dermatitis appeared first in frequency of skin eruptions of the natives in this area. Conditions that could be labeled eczematous dermatitis were present in 23.7 per cent of all those presenting skin conditions. In a large number of cases, the dermatoses were due to contact with weeds or other plants or trees, tough shoe leather or many other agents, including fertilizers and insecicides. Chief among the plant sensitizers were guao, mugwort, mottled spurge, slipper plant, pica-pica and such agents as mango, cashew nuts, creole lemon, mahogany, baywood and cocobolo. Pineapples, tobacco leaves, sugar cane, rice hulls and many other products were mentioned as causative agents by some patients. Dipping solutions for cattle, fertilizers, chicken insecticides, tobacco insecticides, insect bites, lime paint for fences and barns and charcoal making were also thought to be original offenders. Imperfectly tanned shoe leather caused reddish discoloration and dermatitis of the feet. Shanon and Sagher[210] reported an occupational dermatitis caused by sabra fruit (prickly pear) in patients con-

cerned with picking, distributing and selling the product in Israel. This apparently is not a true dermatitis but is due to the prickles or glochidia on the fruit. Patch tests were negative.

Passenger and others[161] studied the effect of an alum precipitated pyridine-ivy preparation called aqua ivy. There have been many reports on the usefulness of prophylactic therapy of ivy dermatitis with aqua ivy. Although the presence of antibodies has not been demonstrated in man and decrease in skin reactivity has not been noted, it is thought that a refractory state can be produced in patients previously sensitive to Rhus. Knowledge of the mechanism of production of this refractory state is lacking. It is known that American Indians chewed the young tender leaves of poison ivy plant because of its beneficial effect in preventing ivy dermatitis. Many workers have used either the oral ivy oleoresin diluted in corn oil or injections of various extracts of Rhus. Toxicity studies in the guinea pig were recorded. There was no evidence of renal lesions following the use of this extract. Since it is difficult to evaluate the results of treatment, the authors were critical in recording results. However, in 63 courses excellent prophylactic results were obtained in 52 per cent of cases, in 50 courses good results were found in 41 per cent and in 8 courses poor results were recorded in 7 per cent. The phylactic use of aqua ivy was also mentioned. It was thought that since it is alum-precipitated and very slowly absorbed, this preparation may be used phylactically in small doses of 0.1 ml. of 1:50 aqua ivy every second or third day subcutaneously without the production of a flare in most cases. While phylactic treatment has been replaced by the use of steroids, evidence is given to indicate the general safety of aqua ivy.

Gaillard[79] does not believe that oral prophylaxis of poison ivy has been effective. Three types of preparations now available for treating Rhus dermatitis are: a solution of poison ivy resin in alcohol; a solution of the resin in almond, corn, peanut or sesame oil, and the active principle in a pyridine-alum precipitate suspended in saline solution. This last material, aqua ivy, can be given without producing pain and the syringe and needle are easily cleaned by washing with water. Gaillard treated 113 patients with this antigen. Satisfactory results were obtained in 77 per cent after the first season, and in 84 per cent after the second season. Of 13 patients treated for three seasons the dermatitis was successfully controlled in 12. Patch tests were made with alcoholic ivy extract using a 1:10,000 dilution of a 10 per cent extract. Dilutions of 1:1000 and 1:100 were also used. Highly sensitive patients were given 0.2 ml. of the 1:50 (0.2 per cent dilution of aqua ivy) followed by 0.5 and 0.8 ml. Patients who were less sensitive were able to take 0.5 ml. of the 1:5 dilution of aqua ivy. Boosters may be given at two to three month intervals.

In response to a query[174] on prophylaxis of ivy poisoning or sensitivity, it was noted that pentadecylcatechol has been used by Kligman at the University of Pennsylvania Medical School in the prophylactic hyposensitization of persons sensitive to poison ivy. This agent is not yet available through commercial channels. There is no indication that prophylactic administration carries any risk of producing glomerulonephritis. The reviewer has had considerable experience with aqua ivy (Strauss Laboratories, New York, New York) and has had no difficulty with regard to the standardization and clinical use of this preparation. In the series of 1,000 patients reported by Epstein and Kligman,[67] eosinophilic pneumonitis developed in 7 patients during the course of therapy

with 3-pentadecylcatechol. Studies showed patchy pneumonitis, leukocytosis and eosinophilia. It was the impression that the pulmonary infiltrates resulted from the trapping of eosinophils in the lung and were not due to any allergic pulmonary reaction.

In another response to a query[176] on prophylactic treatment for ivy poisoning, the use of large amounts of crude oleoresin by oral ingestion was suggested. The Graham Laboratories in Dallas, Texas, make a reliable preparation for oral use and furnish detailed directions for hyposensitization. In differentiation of blisters due to poison ivy from those due to phenylmercuric acetate which appeared on the hands of the patient, Baer[11] noted that primary irritant blisters are more likely to be large and resemble a burn. Furthermore, the blister fluid of primary irritants consists almost exclusively of polymorphonuclear leukocytes. In allergic sensitization such as poison ivy dermatitis, the blister fluid should contain 40 per cent or more of mononuclear cells (lymphocytes and monocytes).

Epstein and Claiborne[62] found some interesting data in the study of racial and environmental factors in susceptibility to Rhus dermatitis. Positive patch tests to Rhus were reported as follows: in Caucasians, 31.2 per cent; in Negroes, 22.1 per cent; in American born Chinese, 21.4 per cent; in China born Chinese, 1 per cent; in American born Japanese, 35 per cent; in Japan born Japanese, 0 per cent; in American born Filipinos, 18.4 per cent; in Philippine Islands born Filipinos, 0 per cent; in American born Hawaiians, 27.9 per cent; born in Hawaii, 4.3 per cent. It is evident from these figures that orientals who were foreign born had little or no sensitization to Rhus. It is possible that these patients may have been immunized by exposure to lacquer plants of the Far Orient or more potent immunizers such as the mango of Hawaii, which are also members of the Rhus family. Those interested in the chemistry of poison ivy should read a review by Dawson,[55] who traces studies and experiments with the ingredients of poison ivy from its early beginning. From recent work, a crystalline saturated component (hydrourushiol or 3-pentadecylcatechol) known as PDC has been developed which is available synthetically and is a valuable standard agent in clinical investigations, such as patch testing of patients with poison ivy sensitivity.

Canizares and Trilla[36] discussed 2 cases of sensitivity to ragweed oleoresin. It was noted that this dermatitis is due to the oil or oleoresin fraction which exists in the outer coating of the pollen and in the leaves and stems of the ragweed plant. As with most patients who have acquired ragweed oil hypersensitivity, there were very few spontaneous cures, and some patients had had ragweed oil dermatitis for over twenty-five years. The oral method of desensitization with ragweed oleoresin results in good control. Desensitization was effective in weed dermatitis, but usually failed in other types of contact dermatitis. Actual contact with the ragweed plant is not necessary to produce ragweed oil dermatitis since sufficient oleoresin clings to air-borne pollen to cause dermatitis in sensitive patients. An antigen, aqua ivy, seems successful in the desensitization of poison ivy. It was noted that a ragweed oleoresin prepared in the same way as aqua ivy may soon be available. This is an alum precipitate of a pyridine extract of oleoresins. It was emphasized that patients sensitive to ragweed oil do not necessarily have an atopic background.

Goldman and others[85] reported that while dermatitis from common English ivy is known to botanists, it is not familiar to dermatologists. This common ornamental plant can cause dermatitis, not only from its

leaves and stems but also from its roots. The dermatitis clinically may resemble that from poison ivy. There is, however, no botanical relationship between English ivy and poison ivy.

Klauder and Kimmich[117] presented an excellent review of sensitization dermatitis to carrots, with special reference to other members of the Umbelliferae family which include anise, fennel, caraway, dill, coriander, parsnip, turnip-rooted celery, pascal celery and parsley. The important publications dealing with these agents are listed and in addition the sensitization and exposure of patients to plants, with subsequent exposure to sunlight, brings up the problem of phytophotodermatitis and its relation to certain botanical species. The Umbelliferae are known to cause dermatitis and to exert photodynamic action. The Rutaceae are second in importance in their capacity to photosensitize. They include the common rue Dictamnus albus, also called "gas plant" and burning bush, and all of the citrus fruits. Several varieties of lime and bergamot are capable of photosensitizing. Other botanical families include the fig, buttercup, bindweed, mustard, agrimony and milfoil or common yarrow. The edible umbellifers—carrots, parsnips, parsley, celery (including celery salt), and turnip-rooted celery—should be considered in causation of dermatitis of the hands of housewives. They should also be considered in cases of cheilitis and perioral dermatitis.

Dermatitis of the hands remains a baffling problem and any contribution is worth scanning. Baukus and Gohringer[13] reported that in 20 per cent of cases occupational dermatitis is the result of sensitivity and the remainder are due to contact with primary irritants, acids, alkalis, solvents and oils. "Do it yourself" programs are responsible for many persons handling potential offenders, such as paints, varnishes, oils, glues, plastics, and others. Housewives are a special problem because of the many potential offenders they use, such as soaps, detergents, cleansers and polishes. Once the dermatitis begins, secondary sensitizers may appear. A brief outline of treatment using standard procedures is given. Soaps are forbidden in cases of hand eczema; Aveeno or raw oatmeal can be used for cleansing.

Grolnick[90] discussed occupational contact dermatitis. The common sensitizing substances were classified as follows: botanical group; cosmetic group; dyes, soaps and washing materials; clothing materials; metals; drugs; insecticides; oils and resins; rubber compounds; industrial dermatitis and miscellaneous substances. Atopy does not necessarily predispose to contact sensitization. The incubation period varies with the subject and with the sensitizer. In industry the individual receives multiple exposures at regular or irregular intervals. At some time in this sequence sensitization begins and the clinical manifestations appear, depending upon the incubation period established for that particular contact agent. Repeated patch tests with some agents may result in a general sensitization of the skin surface, and this practice should be discouraged. According to Morris-Owen,[153] in 5 cases of contact dermatitis due to penicillin or streptomycin, it was possible to depress skin reactivity by daily injection of tiny amounts of the antibiotic agent. Tolerance was noted after some weeks of this type of treatment.

Canizares[34] described a manicurist in whom dermatitis developed from the acrylic materials used in the application of artificial (plastic) nails. Repeated contact with acrylic materials, especially with the sensitizing liquid monomer, is known to be responsible for contact dermatitis in dentists and dental technicians. The sensitizing agent in the case reported

was the liquid monomer of methyl methacrylate. The patient wore a dental plate without eruption or discomfort. Lane and Kost[123] described the case of a 44 year old housewife who applied Patti-nails with an adhesive substance containing various monomers. These investigators found a positive reaction to the powdered polymer, which is at variance with the report of Fisher, who noted an allergic sensitivity to the liquid monomer (methyl methacrylate). In this connection, Tuft and Santor[233] reported stomatitis from allergy to an acrylic denture in a 63 year old woman who had swollen gums and burning and tingling sensations of the tongue following the use of an artificial upper denture. They verified the work of Fisher. Application of the denture to the skin as a means of obtaining a positive patch test should be avoided because reactions are often due to pressure rather than to specific hypersensitivity.

Peck and Palitz[164] discussed sensitization to facial tissues and noted that all dermatologists frequently encounter cases of dermatitis that is limited to the eyelids, the circumoral region or other areas of the face where it is difficult to find the etiological agent. In recent years, facial tissues have been impregnated with synthetic resins to make them stronger when wet. Most manufacturers employ urea-formaldehyde or melamine-formaldehyde resins for this purpose. Fifty subjects were selected for study. The results clearly indicated that these tissues are capable of sensitization. In suspected cases, it is important to make a patch test not only with the suspected tissue but also with a 1 per cent solution of formaldehyde (formalin).

In response to a query[175] about sensitivity to rubber gloves by a physician, it was noted that Anode-latex gloves made by the Miller Rubber Company often can be used by patients who are allergic to Neoprene gloves. Gloves are also made from other synthetic rubbers such as Buna N, known as Hicar. Vinylite, Koroseal, and Pliofilm are newer materials used for gloves. It is also suggested that if Anode-latex gloves are soaked for fifteen minutes in a 5 per cent solution of sodium bicarbonate, rinsed thoroughly in clear water and sterilized, they may be less allergenic. This procedure must be done each time before the gloves are worn.

Blank[17] discussed allergic hypersensitivity to an antiseptic soap recently produced. This is a bar soap (Lifebuoy) containing tetramethylthiuram disulfide which reduces the bacterial count of the cutaneous surface and helps to control axillary odor. This antiseptic is the same chemical used by the rubber industry as an accelerator. A number of patients who had been shown to be allergic to this chemical in rubber adhesives were recalled and tested for their sensitivity to the soap and to the specific chemical used in the soap, as supplied by the manufacturer. Five of the 6 patients were considered hypersensitive to this soap, and for this reason further tests were not made. The manufacturer reported that other investigators had not found a high index of sensitivity to the soap and it was their considered opinion that the 6 cases so studied did not prove that any future serious sensitivity would develop from the product. During the past seventeen months reports from the company indicate no more allergic hypersensitivity to this soap than to the same product before the addition of the new antiseptic.

Although nylon stocking dermatitis is rarely seen by the average allergist and dermatologist in this country, patients with this disorder are still seen in England. Calnan and Wilson[32] reported a characteristic pattern for nylon stocking dermatitis which affects the dorsum of the

feet and toes, the backs of the knees and the inner parts of the upper thighs. It is not the nylon thread that produces hypersensitivity, but the dyes that are used.

Friedman[77] reported the case of a 57 year old man, a stock clerk, who had an eruption of the skin on the left breast, of five months' duration, and mild transitory dermatitis of the hand. Patch tests were made to "lead" of a lead pencil, lacquer finish and wood shavings. In twenty-four hours a bullous reaction appeared at the site of the "lead." There is no lead in a "lead" pencil. The "lead" is graphite, which is a form of carbon found in the earth and is nontoxic except for an occasional case of pneumoconiosis. When the patient was careful in handling pencils, he had no further trouble with the dermatitis.

Contact dermatitis to chlorpromazine has been reported by a number of authors. Seville[207] reported 11 nurses and a pharmacist who developed contact dermatitis to chlorpromazine hydrochloride (Largactil) in England. The principal localization was on the hands and especially in the webs and sides of the fingers. Photosensitivity was a contributing factor and the dermatoses cleared when the drug was avoided.

Reyer[188] studied a number of interesting cases of contact dermatitis of the periorbital area which followed adhesive tape strapping of the lower extremities. Each patient had some problem which required corrective strapping of the lower leg and ankle by a chiropodist. In every case, the eruption subsided when adhesive tape was avoided. It was thought that the antigen was either tissue metabolites in the presence of inflammation or these metabolites in combination with bacterial toxins.

Theodore[230] described the management of eyelid eczema under the headings of allergic eczematous dermatitis due to contact allergy; bacterial or fungal eczematoid dermatitis, and certain generalized dermatoses such as atopic dermatitis, neurodermatitis, seborrheic dermatitis and psoriasis in which eczema of the eyelids may appear in conjunction with other cutaneous manifestations. Eyelid eczemas are often difficult therapeutic problems and differentiation into clinical entities is helpful in management.

Notes on Technique and Interpretation of Patch Tests.—Osborn and Tusing[159] described a rapid method for the application of patch tests with the different suspected agents in the study of patients with contact dermatitis. They show how a number of tests may be rapidly placed and, using a wire tube adaptor and Sergitube gauze, how to apply a fairly large number of patch tests. Kligman[118] found that the Johnson and Johnson band-aid makes an excellent patch test agent because of its sticking properties. The skin must be reasonably dry at the time of application. The sticking properties are apparently not affected by sweating or showering.

Kvorning and Svendsen[122] studied the effect of adding a synthetic detergent in patch test studies on patients with known nickel and bichromate sensitivity. One per cent "Teepol," a synthetic detergent of secondary alkyl sulfate, when added to the antigen was found to produce reactions with a considerably weaker concentration than in controls. This study also suggested that patients who show a negative patch test to a suspected agent may show a positive test when Teepol is added to the antigen. This procedure then would uncover cases of minimal hypersensitivity on patch test.

In the past seven years, Von Haam and Mallette[236] have used the prophetic patch test with 292 compounds employed in the rubber and

plastic industries. Alterations in patch test responses may be caused by the fact that the subjects were previously tested with related compounds. The authors found that the skin irritability could be increased quickly in a group of new subjects by giving them repeated patch tests over a short period. The altered skin irritability was quite nonspecific and could be demonstrated with various chemically unrelated nonsensitizing compounds. This nonspecific skin irritability has not been recognized properly in the literature and it constitutes a serious source of errors in prophetic patch test procedures.

Epstein and Pinkus[66] related their experience with a patient who was thought to be allergic to Alternaria since positive patch tests repeatedly were observed with oleoresins from Alternaria and Trichophyton gypseum. It was found, however, that the patient was rubber sensitive and that the acetone in the antigenic fungous mixtures had come in contact with the rubber stoppers on the vials and actually this had contaminated the antigenic solution. The delayed reaction to the intradermal test with Alternaria may also have been due to the patient's rubber sensitivity because the histologic changes resembled so closely those of the rubber patch tests, and some intradermal tests with other molds and fungi produced similar results. This article again points up the importance of Epstein's contribution mentioned in this review. The second case was that of a woman 27 years of age who was being treated for eczema of the external ears and who was found to be sensitive to neomycin. Patch tests with neomycin may be negative in these individuals. Intradermal tests with neomycin gave strongly positive delayed reactions. Epstein referred to this as dermal delayed rather than epidermal sensitivity.

Johnston and Cazort[110] discussed contact dermatitis from the standpoint of study and treatment of a suspected case. A history may be revealing and may rule out the necessity for extensive patch testing. A selected group of common sensitizers includes potassium bichromate, nickel chloride, paraphenylenediamine, aniline black, benzocaine and derivatives, furacin, merthiolate, ammoniated mercury, acetone solution of poison ivy oil, bitter weed oil and ragweed oil, formalin, procaine and Revlon nail polish. The management includes the avoidance of soap, wearing of cotton clothing carefully washed in Ivory or Lux flakes; application of wet dressings, and of 3 per cent vioform cream following the wet compresses. Tronothane lotion and Quotane lotion have been found to be safe medications. The antihistamines locally are avoided, as are the "caine" drugs, "sulfa" drugs, penicillin and furacin. At bedtime, a combination of chloral hydrate, 15 grains, plus sodium salicylate, 10 grains, affords the patient a good night's sleep. ACTH gel or Sterane is used only in severe cases. In discussion of this paper, the use of poison ivy injections while the patient is suffering from a plant oil dermatitis was condemned.

Noojin[156] described the dermatologic management of pruritus. The mechanism of itching was discussed. A number of new antipruritic agents have been developed over the past few years. Thephorin ointment and other antihistaminics have largely been abandoned. Perazil ointment has been recommended for neurodermatitis and anogenital pruritus. Following this, the use of Quotane ointment as well as Tronothane jelly received good reports. The topical use of Cyclaine and Dyclone has appeared more recently. Pruritic dermatoses showed a good to excellent response in 60 to 80 per cent of patients treated. One

hundred dermatologists were polled concerning their preference for one or another of the favored antipruritic preparations. Hydrocortisone and fluorohydrocortisone were the most favored agents. Next in order of preference were shake lotions containing phenol and menthol; wet dressings; Quotane ointment and lotion; colloid baths; x-ray irradiation; Eurax ointment; 1 to 8 per cent liquor carbonis detergens in ointments and lotions; Tronothane cream and calamine liniment. Systemic agents for the control of itching include the antihistaminics, steroids, sedatives, calcium gluconate, procaine, thorazine and serpasil.

ATOPIC DERMATITIS

Lobitz and Dobson[135] characterized the atopic as a patient with many facets. In their evaluation of the individual patient the range etiologically is from the allergic to the psychosomatic; from the winter problems of ichthyosis to the summer problems of the sweat retention syndrome; and from urticaria to eczema. In a patient with atopic eczema the incidence of atopic diseases (hay fever, asthma and eczema) either in the personal or familial history is abnormally high. There is usually a background of infantile eczema in the adult, childhood eczema in the grammar school age; or the adolescent or adult form of the disease is seen (from 13 to 30 years of age). The general pallor of such patients is probably the result of constant cutaneous vasospasm. The skin is drier than the average. Occasionally frank ichthyosis is present. Follicular hyperkeratosis is commonly seen on the extensor aspects. Patients have patterns of a labile cutaneous vascular reaction. Cholinogenic urticaria may occur from either emotional or heat stimuli. This is due either to hypersensitivity or hyperreactivity to acetylcholine and may be identified clinically by its small papular wheal with a large surrounding flare. The itching may be more intense than that of histaminic urticaria. The normal triple response of Lewis and Grant is modified in the atopic skin. The red line of vasodilatation is replaced by a white line of vasoconstriction. At first the axon-reflex flare is still present but if the skin is more severely involved, the white line of vasospasm is the only vascular response that results from stroking the skin. With improvement of the condition, this abnormality may disappear. The hyperreaction to the cold pressor test in atopic dermatitis is almost in the hypertensive range (Eyster et al., 1952). There is a swifter rate of cooling in a cool environment and a delayed rate of warming in a warm environment when compared with normal patients. In response to acetylcholine injected into the skin of these patients, vasoconstriction or a "delayed blanch" reaction develops. Sympathectomy does not alter the reaction. This paradoxical reaction has not been explained. Sweat retention problems are common in this group. Cataracts may develop in 10 per cent of patients with atopic eczema. Furthermore, positive patch test reactions to eczematogenic allergens are of normal or even subnormal frequency in patients with atopic eczema, with the exception of the reaction to 5 per cent solution of nickel which usually results in a pustular reaction. These basic physiologic characteristics of the atopic are essential to the understanding of the allergic and emotional aspects of the disturbance. The greatest success in handling these patients has resulted from a program of acquainting them with the complexities of the disease.

In previous physiologic studies of atopic dermatitis Lobitz and others (1953) had shown that the blood vessels and eccrine (sweat) glands of

the skin of patients with atopic dermatitis gave a normal response to the intradermal injection of epinephrine but a delayed blanch phenomenon of vasoconstriction occurred to acetylcholine, 1 to 10,000 and 1 to 100,000 when injected intradermally. In these patients, therefore, acetylcholine produced a constrictor response rather than the usual vasodilator response. The reason for this was not known. In order to continue these studies, Lobitz and others[136] tried various denervation procedures on the skin of the atopic, which included local intradermal infiltration of the skin with a solution of 1 per cent procaine hydrochloride in buffered isotonic saline solution; "field block" of the skin with 1 per cent procaine hydrochloride solution; the injection of 1 per cent procaine hydrochloride solution intravenously; brachial plexus nerve block, and unilateral lumbar sympathectomy. All subjects were young adults with atopic dermatitis. It was found that total cutaneous denervation does not influence the "delayed blanch phenomenon" to intradermally injected acetylcholine in patients with atopic dermatitis. In this connection it was shown by Illig (quoted by Lobitz et al.) that the majority of patients with atopic dermatitis respond to the percutaneous application of nicotinic acid esters with vasoconstriction rather than with the normal vasodilatation. Thus the paradoxical delayed vasoconstrictor response to known vasodilating agents in patients wth atopic dermatitis is not limited to acetylcholine. Weiss[243] found that application to the skin of an ointment containing 5 per cent tetrahydrofurfuryl ester of nicotinic acid produces erythema within thirty minutes in normal individuals. It has been reported that the reaction is atypical (no erythema or actual blanching) in patients with acute rheumatic fever or rheumatoid arthritis. Patients with various dermatoses have not been studied by Weiss (personal communication—reviewer).

Ratner and others[185] reported a study of allergy in 64 infants and preschool children. They suffered from various allergic disorders including asthma, eczema, hay fever and urticaria. Twenty-seven of the 64 were under 2 years of age and the remainder ranged from 2 to 5 years. In the New York area, no cases of true hay fever occurred before the third year but pollen asthma was found before the third year. A number of patients had a history of episodes of urticaria in the past. Urticaria does not seem to be a fixed clinical entity in children but occurs at infrequent episodes. By the fifth year food sensitivity in children is said to be reduced to 60 per cent. By skin tests, 58 per cent reacted to seafoods, 48 per cent to egg proteins; 46 per cent to cereal grains; none reacted to rice; 28 per cent were sensitive to citrus fruits. Milk sensitivity occurred in 18 children (28 per cent). The majority gave reactions to the whey proteins and less than one-fourth to the casein fraction. Only the latter group required milk substitutes. A number of patients reacting to grass pollen did not give dermal reactions to timothy on skin test. Usually grass sensitivity was accompanied by other pollen sensitivities, but tree pollen sensitivity did exist alone. Although skin tests are difficult to evaluate in this age group it is believed that all positive skin tests, especially in the young, should be considered as evidence of potential clinical reactivity. Infants suffering from allergy should be skin tested early, studied carefully and treated, since the majority respond favorably to an adequate allergic program.

Ratner,[184] in an article for the general practitioner, gave his usual lucid account of allergic factors in infantile eczema. Most infantile eczemas will clear spontaneously by the first year. If eczema persists,

one should be on the lookout for the development of respiratory allergy in preschool children. The author called this the dermal-respiratory syndrome. Children with atopic dermatitis in whom the eruption persists become difficult therapeutic problems. While positive reactions are obtained on skin testing, the allergenic offending substances are usually multiple and are often inhalants and contactants rather than foods, according to Ratner. Antibiotics given orally usually control secondary infection which occurs from time to time in patients of this group who are so predisposed. Precautions against vaccinating atopic children were mentioned. It is felt that some children with atopic dermatitis may have an associated hypothyroidism which is often helped by the use of small amounts of desiccated thyroid orally.

The approach to the problem of infantile eczema was discussed by Buffum.[26] Atopic dermatitis has a selective distribution with lesions that are not sharply outlined but fade out gradually, accompanied by considerable itching. Seborrhea occurs chiefly on the scalp and trunk and may begin in infants less than two months old. Usually the edges are sharp and well-defined, and itching is noticeably absent. While skin tests are difficult to interpret, they occasionally give real help. When milk, wheat, egg, orange juice and peas are omitted, they may be added one at a time at a four day interval if the child's condition has improved. A flare-up of the dermatitis indicates the particular food as an offender. Nutramigen and meat-base formulas substitute for milk. Vioform is suggested for local treatment and an oral antibiotic for systemic effect. About one-third of asthmatic children have had eczema and probably one-third of babies with eczema will develop asthma later.

Leider[127] discussed the difference between seborrheic dermatitis and atopic dermatitis in infants and children. While both of these conditions may have the same distribution, the clinical appearance of seborrheic dermatitis is somewhat different. There is usually less oozing than in atopic dermatitis and its crusts are greasy scales rather than inspissated serum. On therapeutic tests, seborrheic dermatitis yields more readily to simple remedies such as ammoniated mercury, sulfur or Vioform, whereas atopic dermatitis is much more resistant to topical therapy and is perhaps the most difficult condition to manage in the whole of pediatric dermatology. In essence atopic dermatitis is an inflammatory process, and the useful measures, including baths, wet dressings and bland treatment, are described.

The controversy as to whether allergy plays a lesser or more important role in the production of atopic dermatitis is discussed in an editorial by Hill.[95] While the dermatologists quoted in Baer's book (Atopic Dermatitis, 1955) deny the causal role of protein allergens, it is well known that allergists many times have seen patients whose dermatitis is made worse by foods and environmental allergens to which there is specific hypersensitivity. In response to a letter by Tuft in the *Journal of Allergy*, May 1956, Baer[10] replied that although certain physicians may believe in the immunologic management of atopic dermatitis the majority have found this approach alone to be unsatisfactory. In addition to the immunologic approach it is necessary to recognize that the new advances in the knowledge of atopic dermatitis include studies on the disturbances in sweating, in vascular physiology, including skin temperature regulation, and in response to stress.

Baer[8] outlined the management of atopic dermatitis as follows: In mild cases, hydrocortisone preparations, antipruritic shake lotions (men-

thol 0.3, phenol 0.6, benzocaine 12.0, coal tar solution N.F. 6.0, resorcin 2.4, zinc oxide and talc each 20.0, glycerin 10.0, alcohol and water each 35.0), medicated baths, 2 to 4 tablespoons per bath; avoidance of greasy topical medicaments with the exception of hydrocortisone ointment. Systemically, antihistamines can be given; thorazine, 25 mg. three to four times daily; aspirin 0.3 gm. four times a day (determine whether patient is sensitive to aspirin); and papaverine hydrochloride 0.1 gm. four times daily. Strong soaps should be avoided. In more severe cases, hydrocortisone powder 0.3, crude coal tar 0.6 and Sterosan ointment (Geigy) 30.0 can be used. An alternate prescription is hydrocortisone powder 0.3, crude coal tar 3.0 and paste of zinc oxide 30.0. At times one must resort to radiation therapy, and the patient should avoid direct contact with wool, activities that produce sweating, emotional stress and dusty environments. Hospitalization is indicated for intractable cases, and systemic steroid therapy is advised. Successful management is based on a combination of therapeutic approaches, in which the allergic, dermatologic and nonspecific factors responsible for aggravation of the disease are considered.

Many investigators, including Tuft, Jillson, Osborne and others, have indicated that a relationship exists between atopic dermatitis and inhalants. Derbes and Caro[58] reported a case of a 23 year old white woman with a background of long-standing bronchial asthma who was given intensive therapy with dust vaccine. Patches of eczema developed at the sites of injection after several months of treatment. She had never had atopic dermatitis previously. Biopsy showed the histopathologic findings of eczema. In this connection, Strauss and Kligman[223] made some interesting experiments. They selected 8 subjects who gave strong positive tests to one or more atopens, who had a background for the most part of bronchial asthma and of hay fever and who were also sensiaive to Rhus. They made patch tests with pentadecylcatechol, one of the antigens of the poison ivy plant. Strauss and Kligman were able to show that an existing area of contact dermatitis would flare following the intranasal, subcutaneous and surface application of specific protein allergens. In some cases healing was considerably delayed, and through scratching, lichenified plaques developed which resembled localized neurodermatitis. The suggestion was made that protein antigens as found in food, pollens, molds and so forth are not primarily capable of exciting the eczematous or dermatitic reaction, but are secondary offenders that can produce exacerbations in skin which has been damaged previously, whatever the origin of the damage. Strauss and Kligman thought that hyposensitization has a place in such cases of atopic dermatitis, eczema and other dermatitic reactions, but only when it can be clearly demonstrated that an exacerbation follows exposure to the protein antigen. It is not applicable to all patients with atopic dermatitis and, as a matter of fact, should be limited to a very small percentage. The cause of atopic dermatitis is still unknown.

Diamond[59] studied 490 allergic individuals and found 63 (13 per cent) in this series who suffered from atopic dermatitis. He recorded good results with desensitization using very small amounts of inhalant antigens. Markow[142] studied patients with various forms of allergy, including atopic dermatitis, using nasal smears as important evidence of infection, allergy or a mixture of the two. In a child of 8 with atopic dermatitis, the cytology of the nasal secretion revealed 1 + neutrophils and no eosonophils. Nasal therapy with Biomydrin was instituted and the

skin gradually cleared. The cytology of the nasal secretions was also used as a method of study in a patient with angioedema and dermatitis of the hands. Elimination of the nasal infection resulted in clearing of the dermatoses.

Withers and Hale[250] in an extensive review of the subject of food allergy included some excellent references to foods as the cause of various dermatoses. A good survey of food allergy in infantile eczema is included.

Marchionini and Borelli[141] studied 100 patients with atopic dermatitis who lived in Ankara, Hamburg and Munich, in relation to the effects of change of climate. Each patient was studied individually before a change, either to the seashore or mountains, was recommended. It was found that 79 patients benefited from a change in locale. Change to the mountains required the extra precaution of a sojourn at 1500 feet or more if a good result was to be obtained. The patient was required to stay at least six weeks in his new environment before results could be properly evaluated. The reviewer notes that some years ago it was fashionable to send patients with atopy to certain sections of Texas until the dermatologists and allergists in that area publicly announced that they were overloaded with difficult conditions which did not respond to the climate in that area. Patients should be thoroughly studied allergically and psychosomatically before a climate change is recommended. It was further urged that patients be warned in advance that if they did not do well in one area, they might have to try various sections in the country, either high altitude mountainous areas or warm seashore areas.

Physicians who manage atopic dermatitis often see patients with lesions described as nummular eczema. Such lesions are not uncommon in atopic children. Weidman and Sawicky[240] made a survey of 516 case records and follow-up of 125 patients with nummular eczema. They also reviewed the literature on this disorder. In a study by Fowle and Rice (1953), the incidence of hay fever, asthma, migraine, urticaria and infantile eczema in patients with nummular eczema appeared with slightly less frequency than in patients with contact dermatitis. This speaks against the classification of true nummular eczema as an atopic dermatitis. It should be mentioned, however, that nummular eczema-like lesions are not an uncommon atopic manifestation in children. Essential findings in this study indicated that nummular eczema is most frequently encountered in the younger and middle-aged groups, about equally divided between the sexes. The dorsa of the hands and fingers and extensor aspects of the forearms are most commonly involved, legs and thighs less commonly, and the trunk and face infrequently. Patients experience exacerbations in the colder months of the year and are better in the summer. Seventy-five per cent of the patients tested were sensitive to potassium iodide and 72 per cent to potassium bromide (patch tests). Control groups showed sensitivity to potassium iodide in 47 per cent and to potassium bromide in 26 per cent. Eleven per cent of 125 patients who had a follow-up gave a history of hay fever, asthma, or atopic eczema. For treatment, the most satisfactory topical remedies were Vioform, tars in the form of pastes and ointments. Burow's compresses and shake lotions were of secondary importance. Topical hydrocortisone in combination with antibiotics may prove to be among the most effective remedies. Nummular eczema may be simply a symptom complex.

Rappaport[183] studied melanin distribution and dopa-oxidase reaction in atopics and showed that the cytoplasm of epidermal cells does not

contain pigment during the acute phase of atopic dermatitis. The melanocytes in areas of active dermatitis give a stronger dopa reaction than those in healed sites or in uninvolved skin. Failure of pigment storage in epidermal cells is related to the degree of intracellular and intercellular edema of the epidermis. In involved skin, melanin flows directly into the dermis and is ingested by chromatophores. The uninvolved skin of patients with atopic dermatitis showed an increase in pigment storage within the basal cells.

Smith[217] reported the effect of Sandostene (1-methyl-4-amino-N-phenyl-N-[2-thenyl]-piperidine tartrate). A small group of patients with contact dermatitis, atopic dermatitis and urticaria were treated with a mixture of Sandostene, 12.5 mg., and Neo-calglucon, 1.353 gm., in syrup form. Excellent results were reported. Ampules of this material were used for 5 patients, from 35 to 50 years of age, who had severe eczema. Injections were given every two days; no more than 3 injections were given to any one patient. Relief of itching was almost immediate, followed by improvement of the eczema. The reviewer notes that he has used these ampules for about a year, with rather indifferent results, or at least with results not much better than with the old Neo-calglucon ampules without Sandostene. In some cases patients were treated daily for three to five days, but in many cases it was necessary to resort to other measures in addition to Sandostene plus Neo-calglucon. However, this antihistaminic plus calcium should be tried in addition to other measures to control eczematous eruptions, atopic dermatitis and urticaria.

Morginson and others[151] used a new topical antipruritic agent called Dyclone Creme (dyclonine hydrochloride, 1 per cent, in a nonionic vanishing cream vehicle), testing 222 patients suffering from pruritus caused by 31 skin diseases. Fifty-seven per cent obtained good results and 43 per cent were failures. Abnormal or untoward reactions occurred in 3.6 per cent. *In vitro* studies with this agent showed bactericidal and fungicidal properties, and solutions of dyclonine are self-sterilizing. Patients who experienced untoward reactions had negative patch tests. No signs of toxic reactions or allergic sensitivity were noted.

Clyman[45] reported that hydrocortisone and coal tar preparations in combination are more effective than either agent used alone. Twenty-three patients with atopic dermatitis were studied by paired comparison tests. The cream contained 0.5 per cent hydrocortisone and 5 per cent coal tar extract. Sensitivity reactions were very few. Hutner[103] used oxytetracycline-hydrocortisone ointment in a group of 291 patients. In this series, 129 patients had atopic dermatitis. The response was excellent in 102, fair in 16 and poor in 11. Seven of 8 patients with nummular eczema had an excellent response.

Grayson[86] reported his experience with a new antiseptic "soapless soap" which is an anionic (alkyl aryl sulfonate) detergent bar called Lanolin-Foam. Fifty-four patients with various dermatoses were treated. The detergent bar when dissolved in water forms a solution with a pH of 6.9. It was found to be nonirritating to patients with atopic and contact dermatitis, nummular eczema and exfoliative dermatitis. Swanson[227] reported his experience with a mild neutral detergent soap (Dove) studying 50 patients with atopic dermatitis, including infantile eczema. Ninety-two per cent of these patients, including those with dry skin, could tolerate the soap. Of patients with eczematous eruptions, including contact dermatitis, nummular eczema and housewives' eczema, 74 per cent improved. The lather of this soap is essentially neutral (pH 7)

in contrast with soaps that give lathers with an alkaline reaction (up to pH 10).

Robinson and others[190] treated 36 patients with extensive atopic dermatitis using Atarax in varying dosages from 10 mg. to 25 mg. four times daily. A high percentage of the patients with atopic dermatitis improved, based on objective evaluation of a clinical increase or decrease in erythema, excoriations and the extent of lesions. A comparative study was also made between Atarax and a number of common sedatives or tranquilizers. In most instances Atarax was superior or equal to such preparations as meprobamate (Miltown) and was found to be superior to chlorpromazine. While the drug is given essentially for the relief of tension, secondary improvement of the skin eruptions occurred.

In a discussion of neurodermatitis treated with thorazine, Cornbleet et al[51] noted that 6 patients suffering from the most severe pruritus were treated with Thorazine without any beneficial effect. Serpasil is said to be a good substitute for phenobarbital.

Byrd[29] discussed the psychosomatic aspect of atopic eczema and stated that many persons use their skin as a principal organ of expression. Urticaria may break out when they try to hide excitement. Eczema may be precipitated or continued by the stress of unrelieved emotional conflict. Under the emotional surface of the eczematous patient there is a combination of bitter anger, an anger, however, of which they are ashamed and afraid, and which they often are completely unable to express. Byrd believes that the eczema becomes a part of the patient and is incorporated in the patient's life. It helps him achieve some sort of equilibrium. The opinion was expressed that if the dermatitis is removed, it may throw the patient out of equilibrium and into something that is even worse. Thus, psychologically, one of the best things dermatologists do is fail to cure the patient. The reviewer feels that there would be many who would take exception to this last opinion of this psychiatrist. Many patients have long periods of remission from atopic dermatitis without any major psychiatric catastrophe. I have records of a small number of atopic patients who have attempted suicide, successfully in some instances and unsuccessfully in others. Analysis reveals that the patients were suicidal in spite of their atopic dermatitis.

Kraft and others[119] studied a number of allergic patients from the standpoint of psychotherapy and in this group there were 14 patients with atopic dermatitis and 8 with urticaria. Methods used in the psychotherapeutic regimen are outlined; however, there is no classification of the results according to cases in this paper. Of 75 patients with various allergic disorders, 19 reported no physical improvement, 41 were decidedly improved, and 15 became symptom free. Marmor and others[143] made a study of the mother-child relationship in 22 young children with atopic dermatitis. This study revealed that neglect of the child in the form of separation from the mother or too rough or insufficient handling of the child was present in all cases. Projective psychological studies in 10 of the mothers revealed that they were all emotionally immature women, consciously or unconsciously hostile to their husbands, and frustrated in their self-expressive needs. The theory is advanced that neurodermatitis is a disorder of adaptation—a reaction to stress—in which hereditary, psychological, and physiological factors are operative. Abramson[2] described a case of psychogenic eczema in a child of 4½ years. Her lack of progress was definitely correlated with emotional factors that involved open rejection by the mother and a traumatic experience with

a pediatrician. Coincident with reacting with hostility toward the pediatrician and with the appearance of normal aggression toward the mother, the eczema again disappeared.

URTICARIA AND ANGIOEDEMA

Bolam and Burtt[20] studied 30 English children who had persistent papular urticaria. The ages varied from 3 months to 7 years. Dust samples collected in the homes of 21 of the children revealed fleas. Most of the fleas were identified as animal species. Pets were kept in 20 of the homes. Measures to control the fleas resulted in clearance of the eruption in 14 of the 21 patients. The reviewer notes that this problem has previously been studied thoroughly by Bertram Shaffer of Philadelphia whose reports antedate by many months this present report from England.

Rajka[180] studied the pathogenesis of urticarial inflammatory pruritus. He produced local pruritus by the injection of morphine into the skin and suppressed it by a variety of drugs. He concluded that pruritus is the result of a biphasic mechanism, the first part being an axon reflex comparable to that producing the hyperemic flare after histamine and the pilomotor reflex after nicotine. The reflex then liberates into the tissue an endogenous itching substance which affects sensory nerve endings and this secondary stimulus is transmitted to the brain where it is perceived as itching.

In 3 patients with cholinogenic urticaria, Herxheimer[94] observed that the cholinergic fibers responsible belong to the sympathetic nervous system. When hexamethonium was used to produce a general sympathetic block, urticaria was almost completely prevented. In addition, unilateral cervical sympathetic procaine block prevented urticaria. Local axon reflex sweating in these patients was followed by wheals in the region of stimulation. Although Lewis believed that histamine was responsible for urticarial lesions, the intermediary steps between liberation of acetylcholine at the nerve endings in the skin and the appearance of urticaria are not known. It is well known that antihistamines and histamine liberators have clinical effects on urticaria. The key to the problem may be in the function of the sweat gland since sweat may act as a histamine liberator. Magnus and Thompson[140] studied 6 patients with cholinogenic urticaria and pruritus and found that cholinesterase levels were reduced. It is not possible to state at what level of the skin this occurs.

It is well known that mast cells found in urticaria pigmentosa contain high concentrations both of histamine and heparin. Gardner and Tice[81] studied tissue material from a boy who developed an urticarial eruption at the age of 2 months and who finally died as a result of intraperitoneal hemorrhage at 5 years of age. High levels of histamine were found in the liver and slightly less in the spleen. An explanation for the symptomatology in urticaria pigmentosa might be congenital overproduction or underconsumption of either histamine or heparin. The evidence to date indicates that in urticaria pigmentosa there is excessive concentration of an intracellular organic acid (heparin?). The increased values for tissue histamine are believed to be a homeostatic compensatory overproduction of this organic base in an attempt to "neutralize" the excessive heparin-like organic acid.

Smith and Skaggs[216] studied a number of patients with various allergic diseases for C-reactive protein reactions. Thirteen patients had generalized urticaria, 8 had a moderate number of wheals and the remainder

had either angioedema or mild urticaria. It was found that patients with widespread urticaria had a significant C-reactive protein level, although 2 patients with generalized urticaria had no detectable C-reactive protein. In one of these patients a test forty-eight hours later was 4+. The cause of urticaria was not known in 25 of the 29 patients; 2 had penicillin reactions and 2 serum sickness reactions. The blood of these patients contained large amounts of C-reactive protein. The significance of the C-reactive response in allergic disease is unknown at present.

Wirtschafter[247] and others reported a study of a 42 year old man who showed the phenomenon of cold allergy manifested by urticaria, mottling of the skin and pruritus associated with a cold-precipitable serum protein fraction. Treatment with cortisone abolished the abnormal reaction to cold and resulted in the disappearance of the cryoproteinemia. Cryoprotein was demonstrated by withdrawing venous blood in a warm syringe. This was placed in an oven and allowed to clot. After several hours the supernatant warm serum was decanted and placed in a sterile, graduated test tube and then refrigerated at 5° C. (41° F.). Within two to three hours a white flocculant precipitate could be distinguished throughout the serum; after three days most of this settled to the bottom of the container.

Rapaport[182] reported the case of a 50 year old seaman of Filipino origin who had swelling of the face, hands, lips and mouth on exposure to cold. Various tests were done including search for cryoglobulins, the results of which were found to be negative twice (done before and after exposure to cold), and for cold agglutinins, positive 1 to 16 dilution on the first test and 1 to 2+ dilution on the second test. R. L. Baer, in discussion, stated that four conditions must be considered in cases of cold hypersensitivity: (1) cryoglobulinemia, (2) paroxysmal cold hemoglobinuria, (3) cold hemagglutinations, and (4) essential cold urticaria. Paroxysmal cold hemoglobinuria may occur in syphilis, which was present in this case. There are five major theories as to the pathogenesis of cold urticaria. (1) It may be a true, primary allergy based on an antigen-antibody reaction. Evidence is cited that many investigators have succeeded in passively transferring the disease. (2) The second theory is that a secondary physical allergy exists whereby a physical stimulus, such as cold or heat, produces certain chemical or physicochemical alterations of proteins so that secondary antigens are produced in the tissue to which the organism may become sensitive. (3) The third is that a histamine or histamine-like substance is released. Histamine may be a by-product of a tissue reaction, whatever the primary cause may be. (4) Cold urticaria may be a "cold-specific vasomotor neuropathy" or a "cold pathergy." It is presumed that an instability of the central or peripheral vasomotor mechanism exists which is brought about by some previous inflammatory disturbance caused by bacteria. (5) Duke favored the last theory which is that a central disturbance of the temperature regulating mechanism causes pathologic reactions in the blood vessels of the skin.

Wiseman and Adler[249] reported the case of a 35 year old male baker who had recurrent bouts of hives on the uncovered parts of the body following exposure to cold. Dermographism was not present but when an ice cube was applied to his skin for from three to five minutes, an urticarial lesion quickly formed. This could not be transferred. Further questioning revealed that the onset of the urticaria coincided with the habit of ingesting large quantities of sauerkraut. The offending agent

seemed to be acetic acid, and 0.1 per cent acetic acid introduced intradermally resulted in a definite urticarial response following the application of an ice cube to the skin test site. Controls gave negative results.

In a discussion of solar urticaria, Rostenberg[194] expressed his objections to the term physical allergy. He believes that various reactions recorded to light exposure are the result of some abnormal trait in the individual. Urticaria elicited by bands less than 3700 Å can be reproduced in a normal subject by passively transferring serum from a patient with solar urticaria. This does not happen in the blue violet portion of the spectrum (4000-5000 Å). A suggestion was made that chloroquine or large doses of para-aminobenzoic acid may often protect patients who have solar urticaria.

Gumpel and others[92] reported generalized urticaria associated with acute serum sickness in a 31 year old white man following administration of tetanus antitoxin. Symptoms were delayed for thirty minutes after the antitoxin was injected. Essential treatment consisted of l-arterenol (Levophed) given intravenously, starting with 4 micrograms per cubic centimeter at 60 drops per minute. The concentration was increased every ten minutes until the desired clinical response was obtained at a level of 12 micrograms per cubic centimeter at the same rate. The patient also received 25 mg. of ACTH and 500 cc. of glucose intravenously at the same time in the other arm. When l-arterenol was temporarily discontinued, the blood pressure promptly fell to dangerous levels and improved as soon as it was again started.

In a general pediatric practice, Schwartz[204] found 27 children with urticaria over a two year period. Of these, only 5 had recurrences; 3 had more than one. There was no particular seasonal incidence and nothing unusual in the laboratory findings. It is believed that the rarity of recurrence and the lack of blood eosinophilia (as well as the failure to respond to antihistaminics) make it appear unlikely that most urticaria of childhood is due to an allergic response. It may be manifestation of a specific exanthem of unknown but infectious etiology. Why not, then, an allergic reaction to a bacterial or viral agent, notes the reviewer? A concise review of the problem and management of chronic urticaria is presented by Caplin.[37] In addition to the usual measures, it is noted that antihistaminic drugs may often be helpful if the dose is doubled.

Garat and others[80] gave Clistin (carbinoxamine maleate) in a number of allergic conditions and obtained good results in urticaria in 5 out of a total of 9 patients treated. A dose of 8 to 16 mg. of Clistin was required for control.

Another new antihistaminic compound called Buclizine (1-p-chlorbenzhydryl-4-p-tertiary butylbenzylpiperazine dihydrochloride) was studied by Schiller and Lowell[203] in 70 patients with allergic and related disorders. Of these, 6 had urticaria; and the response to treatment showed 2 excellent, 3 moderate and one with slight improvement. While Buclizine is safe, the duration of action in man is relatively short. Daily oral doses of 25 to 75 mg. were given for an average of four months. Significant abnormalities in the hemogram or changes in hepatic or renal function were not produced.

Lipman[134] treated 72 patients with urticaria with injectable ACTH and at times with oral steroids (Meticortone or Meticortelone later in the series), 20 to 40 mg. Of this group, 58 had acute urticaria, 8 had penicillin reactions, and 9 had other drug reactions. Fourteen patients had chronic urticaria. The average recovery time of the patients with

acute urticaria was two and a half days, but it should be noted that in chronic urticaria three months may be required for control.

Dimetane[27] (parabromdylamine maleate) is a new antihistaminic agent which has had a preliminary trial in the clinics of three investigators. The reviewer has appraised the case reports of a number of the patients with urticaria and atopic dermatitis. In some of the patients in this series the urticaria had become refractory to antihistamines. A favorable response was noted in 80.4 per cent of patients with various forms of cutaneous and respiratory allergic conditions.

Mitchell and others[150] noted that the diagnosis and treatment of chronic urticaria by immunologic methods have often been disappointing. A review of the known etiologic agents in chronic urticaria is given, with a review of the recent contributions in the literature. In order to learn more about this problem, a questionnaire was sent to a number of private patients with chronic urticaria seen between 1948 and 1955. Asked about the cause of the hives in each case, 37 of the patients who answered the questionnaire believed that emotional factors were of major significance, whereas less than half that number thought allergy to be most important.

Abramson[1] discussed the psychic factors in allergy and described certain cases of hives in which the emotional factors far outweighed what is known about possible immunologic factors. In dermographism, for example, it is known that emotional factors in some cases plus mechanical tension on the skin produce the hive. Innumerable cases are on record in which hives immediately follow episodes of anxiety or are incident to conflict situations. Urticaria may persist for long periods and in individuals who have no allergic background and in whom immunologic factors cannot be demonstrated by our present methods. Automatic psychotherapy begins when the patient decides to seek the advice of his physician for symptoms of allergy. Following this, reassurance and a simple plan of educative correction with insight can be used. Only 5 per cent of the patients who consult an allergist are suited for reconstructive psychotherapy with insight. This therapy requires special training in psychodynamic techniques.

Stritzler and Samuels[224] described a 50 year old surgeon who had recurrent attacks of urticaria, chiefly of the hands, which was traced to the use of saccharin (crystallose). It is pointed out by Baer in the discussion of this case that patients sensitive to saccharin may also be sensitive to compounds that have an amino group in the para position in the benzene ring; for example, benzocaine, para-aminobenzoic acid and sulfa compounds.

Canizares and Cipollaro[35] described the case of a 36 year old woman who complained of recurrent swelling in the upper part of the face since the age of 12, coincident with the development of severe, painful exophthalmos of the right eye. Studies showed no evidence of tumor or other organic disease of the central nervous system. The cause of the angioneurotic edema was not determined.

Two patients suffering from recurrent hives following exposure to ammonia fumes are reported by Morris.[152] These cases were industrial contacts either to strong ammonia water or to the fumes still present in the clothes of workers who had been exposed to ammonia fumes. In one instance, cortisone was given but it failed to prevent a subsequent recurrence after exposure to ammonia fumes.

One of the reactions of blood transfusion is allergic urticaria associated

with erythema, acute pruritus, edema or asthmatic symptoms. Winter and Taplin[245] found that allergic reactions to transfusions or whole blood may be reduced from 11.3 per cent to less than 1 per cent by the prophylactic oral use of acetylsalicylic acid plus Chlor-Trimeton added to each unit of blood before its administration.

DRUG ALLERGY

Kerlan[114] pointed out that 10,000 new drugs have been introduced since the new drug provisions of the Federal Food, Drug and Cosmetic Act became effective in 1938. The foremost responsibility of those who administer this act is to detail the proper application of drugs as indicated by clinical investigation and other experimental data. Evaluation in this way by a few medical experts of carefully selected cases may give an entirely different picture from evaluation after the drug has been released for nationwide use. In some cases the drug may be used indiscriminately, especially if it is an "over-the-counter" item. In order to improve reporting of adverse reactions to drugs, a pilot study has been set up with the American Association of Medical Record Librarians in cooperation with the American Medical Association, American Society of Hospital Pharmacists and the Pharmacy and Drug Therapeutics Committees of five hospitals to consider methodology for selecting, reporting, coding, evaluating and disseminating such reactions. Kerlan further stated that, based on a single report, little in the way of control may be feasible, but a series of similar reports would serve to bring about a ready basis for better evaluation of a new drug.

Sherman[211] summarized briefly the subject of allergy to drugs and noted that the diagnosis is usually based on clinical observation of acquired sensitivity. Almost any reaction may be produced by sensitivity to drugs, and in severe cases, purpura, leukopenia, hepatitis or fever may result. Drug fever may occur a week or more after the initial use of the drug, may reach 102 to 105° F., is either continuous or intermittent and at times is accompanied by a maculopapular or erythematous eruption. The leukocyte count is normal or slightly increased, and the eosinophil count may be normal. Once sensitization is established, symptoms may appear a few hours after taking a drug. Hepatitis, which is usually accompanied by other manifestations of drug allergy, may be caused by arsenicals, sulfonamides, cinchophen, gold salts or atabrine. Agranulocytosis, leukopenia or thrombocytopenic purpura also may follow the use of these drugs.

Brown[24] discussed the present day methods of reporting drug toxicity and suggested that a more selective attitude would be of benefit. The report of an untoward reaction may unduly undermine confidence in a worthy therapeutic agent, and certainly almost every drug has at one time or another been the victim of such a report. The reviewer notes that although this criticism is well taken, it is still necessary to acquaint physicians with the dangers inherent in each drug and with the methods taken to combat these dangers. This applies more particularly to those practicing in smaller communities at a distance from medical centers. Brown made a detailed study of the sulfonamides, penicillin, the antiarthritis agents and chlorpromazine to show how better reporting of drug toxicity would result in a more informed public and profession. With the recently introduced chlorpromazine, for example, some authors call it a miracle drug and state that no physical harm results from prolonged moderate use, and others state that "an assessment of these

reports is difficult because some are over enthusiastic, premature, uncritical and unscientific, made after a brief clinical trial, while others are hypercritical reviews based on insufficient evidence" (Ayd, A.A.A.S. Meeting, Atlanta, December, 1955). A second part of this paper concerned with suggested techniques for preparation of toxicity reports is awaited.

Wintrobe and Cartwright[246] reviewed publications on blood dyscrasias from the following drugs: mechlorethamine hydrochloride, triethylene melamine, urethane, benzene, busulfan (Myleran), demedesacetyl- methylcolchicine (Demecolcine), antimetabolites and phenylhydrazine. Leukopenia and granulocytopenia sometimes resulted from the administration of aminopyrine, thiouracil, propylthiouracil, methylthiouracil and sulfadiazine, while thrombocytopenic purpura at times developed after therapy with aminopyrine, phenylbutazone, thiouracil, carbimazole, trimethadione, sulfathiazole, sulfisoxazole (gantrisin), tripelennamine (Pyribenzamine), chloramphenicol, organic arsenicals, chlorpromazine and dinitrophenol. Pancytopenia or aplastic anemia has been known to follow administration of the sulfonamides, Sedormid, quinidine, quinine, gold salts, organic arsenicals and perhaps Terramycin, aminosalicylic acid, phenylbutazone and trimethadione. Hemolytic anemia has developed following the use of arsenobenzols, chloramphenicol, mesantoin, gold compounds and trinitrotoluene. This makes an excellent reference list for the allergist seeing patients in consultation who have a blood dyscrasia or other systemic manifestation of drug allergy and a history of exposure to a rarely used drug.

Antipyrine.—Kennedy and others[113] studied the effects of antipyrine, a preparation commonly used in New Orleans, called 666 cold tablets. Reactions to this drug are particularly striking in Negroes in whom the presence of a fixed drug eruption is usually attributed to this preparation. In addition most of the skin reactions consisted of extremely severe bullous dermatoses and one fatality in the series was recorded. Of 9 patients who had had a previous reaction to the drug, the succeeding reaction was more severe and occurred more promptly than formerly. Bullous eruptions from antipyrine are more common in the Negro race than they are in whites. Patch tests were made to a number of coal tar derivatives. In Case 14 only the antipyrine test was positive and it was positive only over the sites of the fixed drug eruption.

Benemid.—Austrian and Boger[7] reported the history of a patient sensitized and subsequently desensitized to Benemid. A total dose of 40 gm. was given for one month to a 65 year old man who had chronic gout. For a time no reactions to the drug were noted. Therapy was resumed ten months later. Itching of the feet, swelling of the face and scalp, and angioedema were seen 30 minutes after ingestion of 0.5 gm. of the drug. Systemic symptoms also were present, manifested by profuse sweating, faintness, pallor, tachycardia and a fall of blood pressure. Symptoms responded to benadryl. Desensitization was accomplished by giving 0.12 cc. of an aqueous solution of Benemid that contained 5 micrograms per cubic centimeter.

Boric Acid.—Fisher[72] received completed questionnaires concerning the use of boric acid in dermatologic practice from 947 (65.8 per cent) dermatologists listed in the Directory of Medical Specialists. Of those

responding, 94 per cent used boric acid in their practice, 71 per cent frequently. There would thus seem to be widely held clinical impression that boric acid exerts a useful bacteriostatic effect in both the wet preparation and the ointment form. Despite the fact that some clinical studies have indicated that pure water or saline solution is as effective as the wet soaks of boric acid or aluminum acetate solution, this rationale for using a bacteriostatic agent seems valid and is obviously widely supported among dermatologists.

Jordan and Crissey[111] reported a fatal case of boric acid poisoning in an adult from the cutaneous use of boric acid compresses in the treatment of an eczematous eruption. They also presented a critical evaluation of the use of this drug in dermatologic practice. A woman of 35 years was admitted to the dermatologic service of the Buffalo General Hospital; death occurred fourteen hours later. She had been given a benzocaine ointment for an eruption on the left ankle. Because the condition had flared, continuous wet dressings of saturated solution of boric acid were prescribed. They were used for a total of about fourteen days at the end of which time she became lethargic. Twenty-four hours before admission to the hospital the patient became comatose. The blood boron levels were 350 mg. per 100 cc. There is an excellent discussion of the evaluation of boric acid in dermatologic practice. Most physicians continue to prescribe boric acid wet dressings and boric ointments and pastes judiciously, without occurrence of undue reactions. In most situations boric acid poisoning appears when either the powder or the crystals are injudiciously used. It is also noted that when boric acid dressings become dry they should be freshened with water, not boric acid solution, since the latter raises the concentration to an irritating point.

Carbutamide.—Ridolfo and Kirtley[189] discussed their experiences with carbutamide (BZ-55), a sulfonamide derivative having the property of lowering the blood sugar level. Thirty-one diabetic patients were treated with carbutamide. In one patient, after three months of therapy with a daily dose of 1 gm., a skin eruption and leukopenia (1900 white blood cells) developed. Findings of a skin biopsy were not considered specific but were compatible with a so-called drug eruption. Eleven days after therapy, the eruption had disappeared and the white cell count returned to normal. Differential counts after recovery showed a transient eosinophilia. In an editorial[60] on the use of orally given antidiabetic sulfonamide compounds it is observed that skin eruptions have occurred with occasional suppression of the white blood cell count as an evidence of toxicity or sensitivity of the new preparation called carbutamide. The reviewer notes that carbutamide has been generally replaced by tolbutamide (Orinase), which is a safer preparation.

Chloral Hydrate.—Christianson and Perry[43] noted that although reactions to chloral hydrate are infrequent, they do occur and may be severe. The most frequent is an erythematous skin eruption in which there is flushing of the face, neck and chest which may spread to the extensor surfaces of the extremities. The eruption usually develops four to six days after administration, rarely later than the tenth day. Hot foods, hot beverages and alcohol intensify and propagate the erythema. Scarlatiniform, morbilliform, papular and erythema multiforme-like eruptions also may be seen after the use of chloral hydrate. Other

reactions include the urticarial, purpuric, eczematous, fixed eruptions, ulcerative, pyoderma-like, and occasionally vesicular, bullous and lichenoid lesions. Christianson and Perry reported 7 patients who had reactions to chloral hydrate. Patch testing and readministration of the drug for test purposes were not done since it was thought that the clinical features and course were sufficient to support the diagnosis.

Chlorpromazine.—Mullins and others[154] observed skin eruptions in 85 patients who were treated with chlorpromazine. Fifty-seven had an extensive or generalized reaction, 18 showed evidence of photosensitization and 7 patients had only an urticarial response. Contact dermatitis was also noted following use of this drug, with eruptions usually appearing on the dorsa of the hands, flexures, neck and face. Drug eruptions to chlorpromazine do not always follow the accepted pattern. Some patients may safely continue taking the drug after the eruption has disappeared for a few days when the drug has been discontinued. No skin reactions were noted in Negroes and generalized reactions were more frequent in women. Patch tests were of no particular value in determining sensitivity in this series.

Theriault[231] presented a case report of a 38 year old woman who was treated for schizophrenia. The patient was given 300 mg. of chlorpromazine daily. Although her condition improved during the first two weeks, acute pharyngitis suddenly developed and she became febrile. Initial blood studies were normal but agranulocytosis soon developed. A dose of 100 mg. of cortisone as well as antibiotics and transfusions was given late in the course of the disorder but she died five days after the diagnosis of agranulocytosis was made. The reviewer notes that no one has established a satisfactory routine for the management of agranulocytosis caused by drugs. All treatment is supportive and it is rare to find a hematologist who is willing to give large doses of steroids early in the course of the disease when polymorphonuclear cells are absent in the smears. Patients whose condition is deteriorating rapidly from penicillin hypersensitivity may be salvaged by vigorous steroid therapy. The reviewer recently saw a patient with a known exfoliative dermatitis to penicillin suffered five years previous to an operation in which the surgeon found it necessary to use penicillin locally in the peritoneal cavity. This was followed in seventeen days by agranulocytosis preceded by urticaria. The patient made a satisfactory recovery with the use of antibiotics and supportive therapy alone (no steroid therapy). In this particular case the judgment of the hematologist was substantiated by the successful outcome.

Holmes and Stone[99] reported the case of a 55 year old woman who was given 25 mg. of chlorpromazine three times a day for three and a half months. On the day of admission, the white cell count was 1,000, with 1 per cent polymorphonuclear neutrophils. A diagnosis of agranulocytosis was made and administration of Thorazine was discontinued. On the second day, the patient was given a pint of blood and cortisone, 100 mg. every twelve hours intramuscularly. Follow-up treatment also included antibiotics. Eight days after Thorazine was discontinued, polymorphonuclear neutrophils reappeared in the peripheral blood and the patient subsequently made a complete recovery. Høvding[101] reported contact dermatitis from exposure to chlorpromazine in professional and particularly nursing personnel who handle the drug. Procedures are outlined to reduce the hazard of this type of sensitization.

Cahn and Levy[30] studied 15 persons in an attempt to determine what specific light factor may be causal for the dermatitis in patients receiving chlorpromazine. Reactions of photosensitivity to chlorpromazine develop only on exposure to intense summer sunlight containing ultraviolet wave lengths of between approximately 3025 A and 2968 A. The patients in this group did not react to hot quartz ultraviolet light, which lacks the spectrum just mentioned. Patients taking chlorpromazine should avoid undue exposure to summer sunlight.

Brill[23] reported a moderate degree of laryngeal edema which developed in a 51 year old man after ingestion of a 25 mg. dose of chlorpromazine. The patient had a history of chronic alcoholism and barbiturate addiction. Four previous doses had been given intramuscularly with no adverse effects. The patient had reported a severe reaction to penicillin several years earlier. About three weeks after that episode, he was given a 25 mg. dose of chlorpromazine orally by someone other than a physician. Twenty minutes later, severe laryngeal edema developed which required immediate hospitalization. His condition was critical for several hours.

The Council on Pharmacy and Chemistry[52] reported 9 cases of blood dyscrasia associated with chlorpromazine therapy. Six additional cases were found in the American and British literature. The manufacturers of chlorpromazine have information of 45 such cases and also reported that approximately four million persons in the United States have been exposed to chlorpromazine since its introduction. Agranulocytosis was the blood dyscrasia most often reported, although in many cases bone marrow studies revealed depression of other cellular elements as well as the granulocyte precursors. In 17 patients the outcome was fatal. Those patients in whom it was recognized early usually recovered after administration of chlorpromazine was discontinued.

Schick and Virks[202] reviewed the side effects from the use of chlorpromazine and reported the case of a 62 year old housewife who was given chlorpromazine for an involutional psychotic reaction. After about six weeks of therapy, the symptoms associated with agranulocytosis developed. She recovered following the use of penicillin, ascorbic acid, 800 mg. daily, and transfusions. There was no evidence of dermatitis or urticaria in this case. A table is presented summarizing 21 cases of agranulocytosis associated with chlorpromazine therapy; 13 patients recovered and 8 died (a mortality of 38 per cent). The concomitant occurrence of jaundice and agranulocytosis as complications of chlorpromazine therapy is fatal in most cases.

Leinassar[128] reported 4 nurses who developed contact dermatitis from handling chlorpromazine. In all cases, generalized skin eruptions of the face, neck and trunk appeared before localization on the hands and forearms. In one case dermatitis at the site of a patch test persisted for three months.

Colchicine.—Hollander[98] reported the case of a 51 year old man who had vesicular dermatitis of both hands and fingers, of six months' duration. This proved to be caused by colchicine which he was taking for gout. The eruption disappeared when administration of the drug was discontinued and reappeared two days after it was resumed. The dosage was one tablet of colchicine (1/100 grain or 0.6 mg.) every hour for three doses and then one tablet three times a day.

Diamox.—Spring[219] reported the case of a 50 year old woman with hypertension and cardiac failure who developed an itchy papular eruption

on the arms and legs after one week of Diamox therapy. Repetition of Diamox therapy was followed by urticarial wheals. In one patient the eruption cleared after appropriate steroid therapy and in another the eruption cleared spontaneously in spite of continued medication with Diamox. Reisner and Morgan[187] noted the development of thrombocytopenia following the use of Diamox in an 85 year old white man. The clinical findings were severe, bloody diarrhea and a generalized petechial skin eruption, most pronounced on the lower extremities. Platelet survival in plasma was decreased by the addition of Diamox but it had no effect on platelet levels in normal plasma. In purpura caused by Sedormid, quinidine and quinine, it has been shown that the drug in question combined with some factor peculiar to the patient's plasma to produce an antiplatelet agglutinin. Ackroyd (1949) and Bigelow and Desforges (1952) have previously discussed this mechanism in Sedormid and quinidine ingestion.

Underwood[234] reported the case of a 73 year old man who was started on a course of treatment with Diamox, using 250 mg. daily from January 20 to February 20, 1955, with excellent control of edema. On February 20 diffuse purpura was noted and a study of the hemogram and bone marrow showed progressive bone marrow depression. Transfusions of fresh whole blood, parenteral doses of penicillin, and hydrocortisone 120 mg. were given daily throughout his illness. In spite of these measures the patient's condition deteriorated and he died. At autopsy a marked generalized petechial eruption with areas of confluent ecchymoses was found. Numerous petechiae were found in most of the viscera and the bone marrow showed marked hypocellularity with an increase in fat.

Dilantin.—The case of a 29 year old Negro factory mechanic who was given 0.1 gm. of Dilantin® three times a day because of a history of 6 convulsions in fifteen months' time is reported by Gropper.[91] Four weeks later, fever and discomfort in the throat developed and penicillin and Gantrisin were prescribed. An eruption which had previously disappeared recurred, became generalized and was accompanied by exfoliation. Following this, generalized lymphadenopathy and jaundice developed. Dilantin was not discontinued until the third day. In spite of all measures, including cortisone administration, the patient died on the tenth hospital day. Autopsy showed widespread areas of necrosis of liver cells, necrotizing hemorrhagic bronchopneumonia, mild, acute hemorrhagic pancreatitis and cholemic nephrosis.

Furadantin.—Stewart[222] and Rowe reported the use of nitrofurantoin (Furadantin) in 112 cases of acute, persistent or relapsing infections of the genitourinary tract. Thirteen patients (12 per cent) had one or more side reactions, consisting of nausea, emesis, chills, fever, eruptions and dizziness. One case of dermatitis medicamentosa was severe, requiring hospitalization.

Gantrisin.—Davis and Tachdjian[54] noted that while undesirable side effects from Gantrisin occur in less than 0.1 per cent of cases, various eruptions as well as agranulocytosis and hematuria have been reported. The authors reported the case of a 77 year old woman who was given Gantrisin, beginning with an initial dose of 1 gm. and followed by 0.5 gm. twice daily. The next day the temperature rose to 103° F. and a maculopapular rash was noted on her back, and over the flanks and the

abdomen. The following day the patient had severe stomatitis and the entire body surface was covered with a severe bullous dermatitis. Although she was in critical condition, she responded to cortisone therapy, parenteral feedings with high-protein solutions and vitamins, frequent saline mouth washes and ophthalmic terramycin therapy. Penicillin-streptomycin therapy was given daily and all bullae were opened and medicated with Polysporin ointment. Green and Early[87] reported the case of a 69 year old woman who developed a purpuric eruption on the legs following the administration of Gantrisin, 0.5 gm. four times a day because of a urinary tract infection. A diagnosis of thrombocytopenic purpura was made following study of the hemogram. When administration of the drug was discontinued, the eruption promptly disappeared and the hemogram returned to normal. In an additional case, that of a 64 year old man, repeated blood transfusions were required for recovery.

Heparin.—Although heparin has been widely used, reports of sensitivity reactions have been uncommon. Bernstein[14] reported the case of a 71 year old man who had long-standing seasonal rhinitis and asthma for which he was given routine desensitization. Soon after his admission to the hospital because of an anterior myocardial infarction, an intravenous injection of 100 mg. of heparin was given. Two weeks later he was given another intravenous injection of 50 mg. of heparin. Within three minutes an anaphylactic reaction developed, characterized by difficult breathing, shock, cyanosis, extreme apprehension and inaudible heart sounds. After recovery, skin tests and passive transfer tests were made. Intradermal tests with heparin in a dilution of 1 to 100 were positive. Studies indicated evidence of true sensitivity to heparin polysaccharide substance rather than to animal protein contaminants. Recovery followed prompt administration of epinephrine in spite of the fact that he had recently recovered from myocardial infarction.

Iodides.—Peacock and Davison[163] discussed various aspects of idiosyncrasy and allergy to iodides administered to asthmatics. Various allergic manifestations, including purpura and periarteritis nodosa, have previously been described following the use of iodides. In this series, 16.1 per cent of 502 asthmatic patients had sufficiently severe reactions to inorganic iodides to warrant discontinuance or sharp reduction of their medication. Signs of true hypersensitivity did not develop in any of these patients. In most instances they were able to tolerate an organic form of the iodides.

Lentino and others[129] studied 800 patients who were to be given urographic mediums. One-fourth or 200 patients were given Neo-Iopax, 50 per cent solution; one-fourth were given Urokon, 50 per cent solution; one-fourth were given Hypaque, 50 per cent solution, and the remainder were given Renografin, 76 per cent solution. All patients were asked concerning a previous background of allergy, and extensive conjunctival and skin tests were made. The authors concluded that ocular and skin testing are unsatisfactory procedures and have no value in determining whether a reaction would develop in a particular patient. Intradermal skin tests are probably of no value in the average patient, but may be helpful in individuals with a positive history of allergy. There was a significantly higher incidence of reaction in allergic patients when compared with the general population. Wise and O'Brien[248] injected

sodium iodipamide (Cholografin) intravenously in 300 patients in order to obtain serial cholangiograms. Reactions of varying degrees were noted in 34 patients, or 11.3 per cent. Skin tests were made using 0.1 cc. of full-strength solution intracutaneously in 28 instances. Of these, the results were regarded as negative in 17 and positive in 11. An additional 94 skin tests were recorded in patients who did not have reactions; the results were regarded as positive in 13 and negative in 81. Although the incidence of reactions was increased in those patients with a positive skin test, the authors seriously question whether the skin test is of any value; in their opinion it is of no practical value. As a practical solution, they administer 20 mg. of diphenhydramine (Benadryl) hydrochloride intravenously before the dye is injected, then inject 1 cc. of the dye intravenously and wait one to two minutes before injecting the full amount. If there is no reaction to the intravenously given test dose of 1 cc., the full amount is injected. This precaution tended to reduce the incidence and degree of nausea and vomiting. All patients were questioned regarding possible allergic background and personal history of allergic disorders.

Various methods have been used to minimize side reactions to injectable dyes for intravenous pyelography. Sanger and Ehrlich[201] studied over 1000 patients using 20 to 25 cc. of the contrast medium (sodium acetrizoate or sodium iodomethanate) together with 1 cc. of chlorprophenpyridamine maleate (Chlortrimeton maleate), 20 mg. The solution was then rapidly injected intravenously and the reactions of patients were noted. A total of 623 patients were given this mixture and 379 were given the dye alone. The results proved that allergic reactions (urticaria, asthma and so forth) were virtually eliminated. No anaphylactic reactions occurred in the series when these mixtures were used. Patients who had previously shown violent reactions to pyelography have little or no trouble when using the above technique. A history of allergy was not found to be a contraindication when this procedure was followed since asthmatics and allergic individuals were not excluded from the series.

Youngblood and others[254] reported the case of a 60 year old man who suffered a severe reaction following the intravenous injection of Urokon. One hour before going to x-ray, he had been given 50 mg. of Pyribenzamine. He denied any allergic symptoms. Urokon, 1cc. of a 70 per cent solution, was injected intravenously without reaction and two minutes later the remaining 24 cc. was injected in about three minutes time. About three minutes later, the patient was found unconscious. Oxygen was given and he began to recover. At the end of five minutes the blood pressure was 130/70 and the pulse had improved. Shortly after, however, in spite of the intravenous administration of Benadryl, Coramine and epinephrine, he rapidly became cyanotic and pulseless, and was pronounced dead twenty minutes after the first injection of Urokon. An autopsy obtained within an hour showed the larynx grossly to be soft and edematous. The posterior nasopharynx contained extremely large, edematous, soft blebs of material immediately beneath the mucosa. The trachea was filled with tenacious, thick, mucoid material which extended to involve the entire trachea and portions of both right and left main stem bronchi. A 66 year old farmer studied after being given 50 per cent Urokon likewise reacted violently about three minutes after completion of the injection; however, he recovered.

Lapides and Boyd[124] reported 1281 consecutive injections of 70 per

cent Urokon which was preceded by the intravenous administration of 50 mg. of Benadryl without the appearance of urticarial, asthma or shock-like reactions. They noted that in one patient, urticaria and bronchospasm occurred.

Isonicotinic Acid Hydrazide.—Walsh and others[238] described the case of a 38 year old seaman who was given isonicotinic acid hydrazide (INH), 100 mg. three times a day, and para-aminosalicylic acid, 4 gm. three times a day, because of advanced pulmonary tuberculosis with cavitation. Nine days later the patient had general shaking chills and a temperature of 101.2° F. He became asymptomatic about eighteen to twenty-four hours after the medication was discontinued. INH was again started and in five days symptoms recurred. After an interval of two weeks 100 mg. of isonicotinic acid hydrazide was followed within several hours by the same symptoms noted on two previous episodes. This case illustrates the shortening of the incubation period in a patient sensitized to INH. It is of interest that in nirvanol sickness, symptoms arise at regular intervals of six to eight days after the ingestion of the drug. Second courses, however, rarely give rise to immediate reactions (Madden, 1932).

Meprobamate.—Reports of untoward reactions to Equanil and Miltown have been currently invading the literature.[181] Symptoms are variable. Levan and Mundy[130] reported the case of a 32 year old woman who noted a flushed feeling, quickly followed by an eruption on the neck, upper arms and trunk, two hours after taking her first 400 mg. tablet of meprobamate. A repetition of the test dose resulted in similar reactions. Shane and Hirsch[209] reported 3 patients who showed curare-like reactions following use of meprobamate. Coma, marked muscle relaxation, absence of reflexes and hypotension were the main characteristics. All recovered. Carmel and Dannenberg[38] reported 3 cases of nonthrombocytopenic purpura due to Miltown. None of these patients had a past history of purpura, allergy or drug sensitivity. All patients recovered, but it is to be noted that reactions occurred after 1 to 3 tablets were administered for the first time. Had the patients continued to take the preparation, irreversible results might have followed. These authors noted that previous studies have shown scattered allergic reactions involving fever, urticaria and angioedema following the use of Miltown. In view of the free use of this drug, including over-the-counter availability, it would seem that patients should be forewarned of the possibility of these reactions. Friedman and Marmelzat[78] found a number of adverse reactions to meprobamate which included general as well as cutaneous effects. From various sources it has been learned that instances of generalized urticaria, the localized fixed drug-type eruption and the morbilliform toxic-type drug eruption have followed administration of meprobamate. The sites of predilection for the skin lesions appear to be the pelvic girdle area, the breast area and the flexor surfaces of the arm. Less commonly involved are the trunk, anteriorly and posteriorly, and the legs. Sometimes the reaction occurred within three to five hours after taking a single dose of the drug. It must be remembered that related compounds, such as mephenesin, have been used for some time, and may have sensitized some individuals.

Neomycin.—Epstein[64] found 9 cases of a peculiar dermatitis due to contact with ointments containing neomycin. The clinical appearance in most instances was that of an insidious aggravation of a pre-existing dermatitis. Applications of ointments containing neomycin usually, but not always, aggravated the dermatitis. Preparations containing both neomycin and hydrocortisone at times appeared helpful. Patch tests with neomycin were either completely negative or only occasionally or inconstantly positive. Intradermal tests with neomycin solutions of 1 to 1000 and 1 to 100 produced papular tuberculin type reactions. Elimination of ointments containing neomycin was followed by gradual improvement or recovery. This form of contact dermatitis is based not on epidermal but on dermal-delayed (tuberculin-type) sensitivity (Epstein).[63] An observation by Robinson (1955) indicated that other antibiotics such as Terramycin may also cause contact dermatitis with negative patch tests.

Novobiocin.—Martin and others[144] gave novobiocin to 34 patients with infections due to a number of organisms. The reaction to novobiocin most frequently seen was an allergic dermatitis consisting of urticaria and angioedema, which occurred in 5 of 34 patients. The reviewer has seen several patients who have had a morbilliform or scarlatiniform drug eruption with fever ranging from 103° to 105° F. after taking 2 gm. of novobiocin daily. One of these patients was reported by James and Stanton.[107] The fever and eruption subsided within twenty-four to thirty-six hours on withdrawal of the drug. In a controlled study, Welch and others[244] studied a number of volunteers to test the sensitizing potential of novobiocin. The study was controlled by a group who received lactose, a second group received penicillin and two other members of this group were given two types of novobiocin. Four of 105 male volunteers showed a drug eruption on an oral dose of 0.5 gm. of novobiocin twice daily for five days. Patients were given a rest period of two days and then the five day course was repeated. A high percentage of skin eruptions due to novobiocin have been reported. Welch et al. believe that if the dosage is kept to 0.5 gm. twice daily, skin eruptions may be avoided.

Nuvarone.—Isaacson and others[105] reported their experience with nuvarone, an antiepileptic drug. Of the well-established hydantoin derivatives, Mesantoin has been the chief offender in the production of cytopenia. Dilantin has been notably free from hematopoietic toxic reaction. In previous studies with nuvarone, it was demonstrated that of 91 patients, 5 had mild changes in leukocyte counts, which responded rapidly to drug withdrawal. Some of these patients had nuvarone alone and others had nuvarone combined with other antiepileptic drugs. The authors reported the first fatal case of pancytopenia after nuvarone therapy in a 37 year old woman. This occurred after the patient had taken this preparation for six months prior to hospital admission. Periodic blood cell counts in all patients using this preparation are indicated.

Para-aminosalicylic Acid.—Alt and Spengler[4] reported the case of a 42 year old man with pulmonary tuberculosis who was given INH, 100 mg. three times a day, and PAS, 4 gm. three times a day. In about a month, generalized myalgia, a pruritic maculopapular eruption and pharyngeal symptoms developed. Symptoms subsided and again recurred

when he inadvertently was given 8 gm. of PAS. After forty-eight hours, a 27 per cent eosinophilia was noted. A patch test with PAS was positive.

Penicillin.—Feinberg and Feinberg[70] pointed out that penicillin has become the primary problem in drug allergy. Three hundred tons of penicillin are manufactured annually in the United States. The cutaneous manifestations of sensitivity include urticaria, various eruptions, exfoliative dermatitis, contact dermatitis, and erythema nodosum and multiforme. Purpura and periarteritis have been reported. A number of papers describe myocardial and renal changes occurring during the serum-sickness type of reaction. More serious visceral changes are accompanied by lupus erythematosus cells in the peripheral blood and marrow in cases of penicillin allergy. The two most important allergic reactions from penicillin are the delayed serum-sickness type and the immediate, anaphylactic type. Both are examples of immediate allergic reactivity, but the delayed type has a temporal reference only. Syringes that had been used for penicillin injections have been demonstrated to retain sufficient allergenically active penicillin to produce symptoms in highly sensitive persons. Cow's milk (subsequent to the treatment of mastitis) may constitute a sensitizing source of penicillin. The amount of penicillin in the poliomyelitis vaccine is small, but judging by its activity as determined by the authors in tests of passively sensitized human skin, it is sufficient to produce reactions in highly sensitive persons. Severe anaphylactic reactions have as yet not been seen following injection of poliomyelitis vaccine in the mass immunization programs. In suspected penicillin allergy, a scratch test with a weak solution of about 5,000 to 10,000 units per 1 cc. is in order. If this is negative, an intradermal test should be made using 0.01 cc. of a solution containing 1,000 units of crystalline penicillin per cubic centimeter. The vast majority of patients who react anaphylactically will show an immediate whealing reaction. In these patients, penicillin administration is hazardous.

Three cases of nonfatal anaphylactic reactions following oral administration of penicillin and one fatal case following intramuscular injection of penicillin are presented by Peters and others.[165] Various skin test procedures are presented that indicate the presence of heat-labile circulating antibody, which may serve to predict potential anaphylactic reactions. The skin test in itself is apparently inadequate as a screening method, but if a pronounced positive reaction to a skin test is found in an atopic individual, penicillin should be avoided.

Weiner and others[241] presented the case history of a 25 year old woman who had had asthma for a number of years. She had previously received penicillin intramuscularly on several occasions. The patient was taking minimal dosage of hydrocortisone orally for maintenance allergic therapy. Oral ingestion of 200,000 units of crystalline penicillin G was followed by unconsciousness, cyanosis and respiratory distress, requiring oxygen, epinephrine and aminophylline.

Krohn[120] reported 3 cases of anaphylactic shock-like state following oral ingestion of penicillin. None of these patients appeared to be asthmatics. Scratch and passive transfer tests correlated well with the degree of clinical sensitivity. Case 3 showed an anaphylactic shock-like state following scratch tests with powdered penicillin G containing 200 and 20 units per cubic centimeter, respectively.

Bierlein[15] presented the case of a woman, aged 55 years, who had a known background of allergic rhinitis and conjunctivitis. She had previously been able to take penicillin by injection and there was a history of oral administration of penicillin. In January 1955 she took a 200,000 unit tablet of long-acting penicillin; within a half hour her eyes became red and edematous and she had generalized pruritus with swelling of the palms and soles. A skin test using fresh dilution bottles, stoppers, syringes and needles resulted in a systemic reaction when 0.01 cc of a test dose of 0.000003 unit of penicillin was given intradermally. A further reaction occurred from dust desensitization when it was shown that the rubber stopper for the dust bottle may have been contaminated by penicillin. This case demonstrates how infinitesimally small amounts of penicillin may produce a fatal or near fatal constitutional reaction in highly sensitive patients. Great care should be practiced to prevent contamination of syringes and needles used to administer parenteral therapy to these patients. As long as poliomyelitis vaccine contains penicillin it may produce anaphylactic shock or allergic reaction in individuals sensitized to penicillin. (Anaphylactic reaction from poliomyelitis vaccine has yet to be reported—reviewer.)

Weinstock and Albin[242] reported a nearly fatal penicillin reaction in a physician. One of the authors (Weinstock), 44 years old, gave himself an injection of 600,000 units of procaine penicillin G into the buttock. This was followed by anaphylactic shock, unconsciousness and incontinence of urine and feces. He was found by the second author (Albin) in this state about thirty minutes later. It was difficult to do venipuncture but this was finally accomplished and 50 mg of ephedrine sulfate and 500 mg. of aminophylline were administered intravenously. This was followed by the first signs of returning consciousness. Oxygen was administered and 1 cc of epinephrine, 1 to 1000, was given intramuscularly. Following this the pulse remained imperceptible. Forty milligrams of Histadyl and 59 mg of ephedrine sulfate were then given intravenously. Although the patient recovered, it took approximately six weeks for him to be restored to his usual state of health.

de Mello and Mendes[149] reported the case of a nurse who had been given over 14,000,000 units of penicillin in 1951 and over a million units in February 1954 without adverse reactions. After June, 1954, severe reactions developed whenever the patient handled penicillin or when she passed by the door of a room in which aerosol penicillin was being used. Symptoms consisted of severe generalized pruritus and urticaria. Patch tests to both sodium penicillin and procaine gave negative results. Four days after the negative results of the patch tests an intradermal injection of 25,000 units per cubic centimeter of sodium penicillin was given. A severe anaphylactic reaction occurred immediately after the injection. Treatment of the anaphylactic shock was described.

In answer to a query[177] regarding allergy to penicillin, it was stated that most of the critical observations and investigations indicate that allergy to one type of penicillin presupposes allergy to other types. The frequency of allergic reactions from penicillin O (Cer-O-Cillin), which may be obtained in oral, soluble injectable and repository injectable forms, has decreased. It is also thought that Compenamine or L-ephenamine penicillin G is also a repository type and shows fewer reactions. The reviewer notes that it would be best to avoid academic and theoretical dis-

cussions of this type of problem and simply avoid penicillin in any case since there is such a liberal choice of suitable antibiotics to be used in most cases. The sudden appearance of an anaphylactic reaction following penicillin in a patient who has a nonfatal disease is something that cannot be forgotten.

In order to study the parenteral and oral use of antihistamines in preventing penicillin reactions, Mathews and others[145] made an extensive controlled study of student groups at the University of Michigan, Student Health Service. A total of 2,299 courses of penicillin were given, using various routes of administration and including a controlled group. Experimental conditions were defined for evaluating procedures influencing the incidence of penicillin reactions. The study failed to show that antihistamine administered orally or parenterally, or both, produced any significant effect on the incidence of delayed or severe penicillin reactions. Early reactions of the urticarial type were reduced. It was found further that penicillin reactors had a significantly higher incidence of moderate or severe local reactions than nonreactors. Often the delayed reactions were more severe than the "immediate" reactions. An exception to this finding, however, is the rare anaphylactic type of reaction which is likely to occur within seconds or minutes after the injection of penicillin. No such reactions were encountered in this series of cases.

Coleman and Siegel[48] studied 9 sera from penicillin-sensitive individuals using the method of contralateral passive transfer reactions. Various amounts of Chlor-Trimeton were mixed with the procaine penicillin in these experiments. The study showed that the addition of an antihistaminic drug to a therapeutic dose of penicillin had no significant deterrent effect on the development of contralateral passive transfers on sites passively sensitized with a serum containing reagins to penicillin. They would, therefore, agree with the study by Mathews and others[145] at Ann Arbor that it would seem unlikely that the admixture of antihistaminic drugs with penicillin would prevent the severe, immediate allergic shock or anaphylactic reaction from developing in the extremely sensitive person. Siegel and Coleman,[212] in continuing their studies on penicillin hypersensitivity, noted that reagins to penicillin have been found in the sera of many patients following allergic shock reactions produced by this antibiotic. Occasionally, however, failure to find antibodies is reported. In order to study this problem further, a number of passive transfer studies were made and the sites tested with brands of penicillin from various companies. This led to a study of the effect of aging of penicillin under various conditions. In addition, it was found that procaine penicillin G crystals freshly suspended in saline solution gave no positive passive transfer reactions when refrigerated for one month or when kept at room temperature for two weeks. It was thought that in view of these experiments there is reason to question the advisability of storing procaine penicillin suspension at room temperature, as is now recommended by the manufacturers, or keeping it in the physician's bag for long periods of time. Refrigeration of penicillin does not promote alteration of its allergenic properties and this type of storage would appear to be preferable. In addition to these factors, failure to demonstrate reagins in some cases may be due to reagins to penicillin disappearing from the circulation within a few weeks after shock reaction.

Nasou and Romansky[155] discussed the various aspects of the complications of antibiotic therapy. Among the complications incident to the host's response, the sensitivity reactions to antibiotics have attracted

the greatest attention, probably because they are the least predictable and commonest. Skin reactions occur particularly with penicillin and streptomycin and are comparatively rare with the so-called broad spectrum antibiotics. Anaphylaxis, perhaps the most alarming complication of antibiotic therapy, is caused primarily by penicillin.

Phenindione.—Pastor and Tetreault[162] reviewed the literature on the use of phenindione, an anticoagulant preparation, and noted that various eruptions have been described. High fever, hepatitis, jaundice and a morbilliform eruption as well as leukemoid blood findings and anemia were previously described. The case is presented of a 33-year-old-man who was given anticoagulant therapy with phenindione (Hedulin) because of myocardial infarction. Cutaneous reaction occurred on the forty-sixth day and by the fiftieth day definite agranulocytosis had developed. Phenindione was discontinued and penicillin, streptomycin and corticotropin were given. The patient recovered uneventfully. It was felt from this experience that steroid therapy had markedly improved the prognosis in agranulocytosis. The reviewer notes that more precise information is needed concerning the role of the steroids in agranulocytosis.

Poliomyelitis Vaccine.—Since some type of reaction was to be expected from the widespread use of Salk poliomyelitis vaccine, an article by Bierly,[16] who is associated with the medical department of one of the largest producers of poliomyelitis vaccine, is of considerable interest. The ingredients of synthetic medium 199 are listed in detail. The essential ingredients of poliomyelitis vaccine include medium 199; horse serum in a final concentration of less than one part in 5 million; phenolsulfonphthalein 0.002 per cent; soluble monkey protein, derived from blood or kidney; antibiotics; formaldehyde 1 to 4000—sodium bisulfite complex; preservatives; poliomyelitis virus protein and nucleoprotein. While a tiny amount of penicillin G is present in all poliomyelitis vaccine, the amount assayed less than 15 units per cubic centimeter in the Wyeth vaccine. It must be remembered, however, that the data developed by Coleman and Siegel (1955) concerning penicillin-contamination of sterilizer water or syringes as a cause of allergic reactions in a severely hypersensitive individual, leave little doubt that the breakdown products of penicillin are antigenic. It was later concluded that the penicillin content of poliomyelitis vaccine is negligible. The vaccine should offer no hazard either to persons allergic to penicillin or as a source of newly acquired penicillin sensitization, according to Siegel (1955). In Denmark in 1955, where 425,000 children received two simultaneous intradermal injections of 0.1 to 0.15 cc each of poliomyelitis vaccine, the reactions were mild and infrequent, consisting mainly of local swelling of the arm at the site of inoculation. The percentage reaction was 0.1 to 0.2 in the preliminary estimate of the children so vaccinated. The reviewer, however, has seen patients who have complained of mild urticaria or erythema multiforme, or both, following use of poliomyelitis vaccine, principally in older individuals. Several hundred adults, some of whom were known asthmatics or who had previous penicillin injections, were able to tolerate poliomyelitis vaccine with little or no reaction.

Chervinsky[42] reported erythema multiforme following poliomyelitis vaccination in a 9-year-old girl. The eruption appeared two weeks after the first injection of 1 cc of Salk vaccine. About a month later, she

was given a second injection of 0.1 cc intradermally. While there was no local reaction, five days later the patient noted joint pains in both knees and shoulders, and generalized severe pruritus. This was followed in twenty-four hours by an erythema multiforme-like reaction. Prednisone, 10 mg every four hours, relieved the symptoms within twenty-four hours, and was continued for one week. It was thought that the most likely cause for the erythema multiforme was some component of the Salk vaccine. The reviewer has seen a similar problem in a 38-year-old woman who had a definite allergic background. The use of intradermal vaccine on two subsequent occasions, however, failed to reproduce the original reaction noted after the injection of 1 cc.

Healy and McDonald[93] reported a rare instance of allergy to protamine in a 62-year-old man. The patient had gone to his physician two weeks before this study and a diagnosis of diabetes mellitus was made. He was given 10 units of protamine zinc insulin daily. The symptoms were chiefly pruritus and angioedema. There was no background of asthma, hay fever or other allergic conditions. Skin tests with protamine were positive and with beef, pork, and crystalline insulin, were negative. The patient was able to tolerate NPH insulin for the control of the diabetes.

Quinine.—A woman allergic to quinine developed thrombocytopenic purpura immediately after delivery. The disorder was also noted in the newborn infant. Mauer and others[146] found that purpura in both cases was due *in vitro* to platelet agglutination in the presence of quinine. Although antibody was still present in the mother five months later, it was lacking in the blood of the infant. It is believed that the purpura was a result of transplacental passage of antibodies as well as quinine from the mother.

Steinkamp and others[221] reported the case of a 31-year-old woman who developed thrombocytopenic purpura following the ingestion of bromoquinine. The symptoms recurred when one-fifth of the amount of quinine present in a bromoquinine tablet was ingested. A normal volunteer, who had previously ingested 500 mg of quinine hydrochloride and took 250 mg more at the time of an injection of 200 ml of plasma obtained from this patient, also developed a clinical picture of thrombocytopenic purpura. Platelets dropped from 850,000 to 20,000 per cubic centimeter. That this effect was not permanent was demonstrated by the lack of reaction in the volunteer after the ingestion of quinine three months later. Passive transfer studies using the patient's serum and quinine gave negative results but apparently the method employed by Squire and others in producing Tolserol transfer was not used.

Bolton and Dameshek[22] studied 5 cases of thrombocytopenic purpura due to quinidine and reviewed cases previously described in the literature. When depressed by the drug, platelets may range from 4,000 to 67,000 but briskly return to normal if the drug is discontinued. Recurrence of a decrease in platelet count may be noted within six hours of a test dose of quinidine sulfate 0.3 gm. Laboratory studies indicated that plasma which was platelet-free from these patients could agglutinate the platelets of normal platelet-rich plasma only in the presence of quinidine. It was shown that complement fixation occurred during this reaction. A reverse test indicated that the serum from a patient who had been given considerable quantities of quinine as well as quinidine could agglutinate the platelets of these patients in the presence of

quinine or quinidine. The presence of purpura which includes intraoral hemorrhagic bullous lesions suggests the possibility of drug thrombocytopenic purpura especially if quinidine is being given. Bolton[21] demonstrated that in a case of quinidine thrombocytopenic purpura an abnormal factor was present in the plasma or serum which caused agglutination and lysis of platelets from normal individuals or from the patient in the presence of quinidine. This reaction did not occur if quinidine was exchanged for quinine. Concentrations of quinidine of the order of 0.3 mg per liter caused platelet agglutination *in vitro*. These experiments are interpreted as evidence of the presence of an antigen-antibody reaction similar to that of Sedormid purpura described by Ackroyd. In neither instance was a PK positive reaction demonstrated. The antibody is apparently a gamma globulin which does not attach itself to the platelets unless quinidine is present. In none of the experiments performed could quinine be substituted for quinidine.

Many observers have reported recently on thrombocytopenic purpura due to quinidine. Freedman and others[75] emphasized that the physician must have a high index of suspicion in cases in which the drug is given and thrombocytopenic purpura develops. The medication should, of course, be stopped immediately. The usual serum factors found in sensitized patients with thrombocytopenic purpura are discussed. There is evidence that a factor with the characteristics of an antibody may occur frequently in the sera of patients with drug-induced cytopenias. The authors suggested that the evidence favors Ackroyd's theory that a single antibody could react with any of the cells in the platelet, megakaryocyte endothelial blood systems in the presence of a drug which acts as a hapten. A convenient screening test in sensitized patients is the inhibition of clot retraction in the blood in the presence of quinidine.

Shands and Johnston[208] reported anaphylactic shock from intrapleural administration of streptokinase-streptodornase, which is known as Varidase. This substance acts by liquefying fibrin and nucleoprotein, thus facilitating the removal of clotted blood from the pleural cavity. Frequent aspirations are advised to provide good drainage. A male patient with an injury to the right chest required the use of Varidase. At the first treatment a considerable amount of serosanguineous fluid was successfully removed from the chest. After the second instillation, the temperature rose to 104° F., and some generalized itching was noted. One week later, and four hours after the third intrapleural administration of Varidase, a severe, fulminating, near fatal anaphylactic reaction occurred. Vigorous treatment with antihistaminics, oxygen, pressor agents, and ACTH intravenously led to recovery. Skin tests were not permitted by the patient.

Sulfonamide.—While the cause of systemic lupus erythematosus is not known, certain constitutional factors, such as age, sex and hypersensitivity reactions to drugs, sera or bacteria as well as sunlight, may precipitate the disorder. Honey[100] reviewed the pathology and symptomatology of this disorder and presented a case of systemic lupus erythematosus in which the disease was preceded by severe hypersensitivity to sulfonamide. A nephrotic syndrome and hypersensitive encephalopathy accompanied the disease.

Thiamine Chloride.—Tetreault and Beck[229] presented the case of a 62-year-old man who was admitted to the hospital with a diagnosis of

mild cerebrovascular accident. In 1949 he had noted flushing of the face, dizziness, palpitation and sharp precordial pain after receiving 1 ml of 20 per cent thiamine intramuscularly. Five years later, at his most recent admission, he was given 1 cc of Betaxin (100 mg of thiamine hydrochloride) intramuscularly by a physician who did not know of the previous thiamine reaction. Within a half hour the patient went into shock. Levophed, aminophylline, atropine and Benadryl were required to relieve the symptoms of shock and bronchospasm. He recovered uneventfully in about thirty-six hours.

Tolserol.—Arkins and others[5] reported the case of a 41-year-old woman who was seen following an acute drug reaction. She had previously been given A.P.C. tablets, Tolserol and tetracycline for an inflamed pharynx accompanied by local muscle tenderness. Approximately twenty minues later, she experienced diaphoresis and numbness of the circumoral region and upper extremity, with tingling and tightness of the chest. On the fourth hospital day 250 mg of Tolserol was given orally and within thirty minutes the symptoms recurred and the blood pressure decreased. She was given 50 mg of Benadryl intravenously and one ampule of l-arterenol and 100 mg of hydrocortisone diluted in 1 liter of 5 per cent glucose in water. Within a few minutes, the angioedema in the circumoral area subsided. A direct cutaneous test with 1 per cent aqueous mephenesin gave negative results. Serum of this patient was transferred to 4 subjects who in forty-eight hours were given 500 mg of Tolserol. In 3 of the 4 test subjects, within ninety minutes after ingestion of the drug marked whealing reactions occurred in sites sensitized with undiluted serum. Skin sensitizing activity could still be demonstrated in serum withdrawn thirty days after the patient's reaction to Tolserol.

Vitamin K.—A case is reported in Queries and Minor Notes[179] of intense anaphylactic shock which developed in a 44 year old woman after the intramuscular injection of 1 mg of vitamin K (Synkamin). Rapid recovery followed the use of epinephrine chloride, 1:1000, and later, caffeine and sodium benzoate.

Sulzberger[226] showed the connection between the skin and adrenal glands. He pointed out that both organs are most intimately concerned with the adaptation of man to his environment and that the immunologic and allergic changes are fundamentally reactions of adaptation. The indications for steroids in allergic dermatoses are classified. It is important to watch the patient carefully for weight gain, changes in psyche, blood pressure fluctuations, urinary sugar and for general physical and mental findings when the patient is taking 75 mg or more of cortisone or its equivalent. Steroids may be used as adjuvants in eczematous contact-type dermatitis, acute urticaria and angioedema, certain drug eruptions (purpuric, urticarial and exfoliative) and erythema multiforme. Prolonged administration of hormones may be necessary in atopic dermatitis, exfoliative erythrodermas, nummular eczema, eczematous eruptions of the hands, distinctive, exudative discoid and lichenoid chronic dermatitis, chronic urticaria, seborrheic dermatitis, psoriasis of the erythrodermic, pustular and arthropathic varieties and particularly in intertriginous areas.

STEROID HORMONES

Wartzki and Entwisle[158] reported their experiences with the use of topical hydrocortisone in 100 patients with various skin lesions. Best results were obtained in erythema multiforme, papular urticaria, dermatitis and eczema of the face, especially of the eyelids, eczema of the scrotum, pruritus ani and vulvae and intertrigo of the genitocrural and gluteal folds. A poor response was obtained in Besnier's prurigo, nummular eczema and otitis externa. Aggravation of the dermatitis was noted in some patients. The reviewer can report a 60 to 70 per cent reduction in the number of new patients seen with pruritus ani and otitis externa because of the widespread use of topical steroid therapy by physicians who first encounter these conditions. The reduction in the number of patients seen with these heretofore difficult and sometimes intractable conditions has been striking.

Wittich[159] used diphemanil (Prantal) methylsulfate cream containing 2 per cent of the agent and Prantal with Cortifan cream containing 2 per cent Prantal with 1 per cent hydrocortisone for a number of dermatoses including recurrent hives, dry skin and eczema. Patients with contact dermatitis, dermatitis due to irradiation and pruritus hiemalis were benefited. It was felt that these anticholinergic creams control the pruritus more effectively than other local antipruritic measures. None of the patients showed any side effects or toxic reactions.

Levin and Sutton[131] treated 108 patients with various dermatoses using a new steroid-antibiotic ointment called Cortisporin. It contains 1 per cent hydrocortisone, polymyxin B (5,000 units per gram), bacitracin (400 units per gram) and neomycin (5 mg per gram). The greatest improvement was shown in patients complaining of pruritus ani, pruritus vulvae, otitis externa and seborrheic dermatitis. Hand eczemas and other eczematous eruptions as well as contact dermatitis also responded to this steroid-antibiotic ointment.

Vollmer[235] reported his experience with 28 children and 3 adults suffering from various allergic dermatoses who were treated with fludrocortisone lotion and ointment using the simultaneous-paired comparison method. About two-thirds of these patients were improved. Undesirable side effects were not observed from this agent, but he notes that Fitzpatrick and co-workers found edema formation and sodium and water retention in patients with dermatitis who were treated with topical applications of fludrocortisone.

Smith[215] studied 40 patients with various eczematous eruptions including atopic dermatitis and concluded that although prednisolone ointment, 0.5 per cent, is of value, it is less effective than 1 per cent hydrocortisone ointment. The ointment base in all preparations was petrolatum and the duration of comparative treatment varied from three days to four weeks. Mild irritation from the prednisolone ointment was noted in 3 patients. There were no allergic contact sensitivities to any of the ointments used in this study.

Hirsch[97] reviewed the use of systemic adrenocortical steroids with special application to dermatology. He particularly stresses the rebound relapse when this type of therapy is discontinued and notes that the steroids are primarily indicated in nummular eczema, contact dermatitis, dyshidrotic hand eczema and sunburn. Chronic lichenified lesions responded better to other modes of therapy. The author lists the following side effects: osteoporosis; portions of or the entire picture of Cushing's

syndrome; exacerbation of quiescent peptic ulcer; dissemination of tuberculosis in an active tuberculous patient; abnormal salt and water retention; increased susceptibility to infection; especially tuberculosis. On drug withdrawal one may see rebound relapse; occlusive vascular accidents, such as coronary thrombosis; and relative adrenal insufficiency due to superimposed stress. Changes of the mental picture, resulting in psychotic episodes, are usually temporary and reversible upon cessation of the drug.

Lipman[134] made a survey of 417 patients with allergic diseases seen over a three-year period. These patients had all received steroid hormones as primary treatment. There were 73 cases of atopic eczema. The age range for these patients was 6 weeks to 73 years, and the average duration of the disease was 7.4 months. History revealed 24 remissions from previous drug or allergy management in this group. With injectable steroids, however, 64 of the 73 patients obtained a remission but the average duration of remissions with steroid therapy was 36.5 days. Thirty-two patients continued on allergy management plus steroids.

There were 113 cases of contact dermatitis.[134] Of this group, the average duration of symptoms was 183 days and the average duration of treatment with ACTH was 10.8 days. Complete remissions were seen in 68, partial relief of symptoms in 34, no relief of symptoms in 11 and recurrence of contact dermatitis after cessation of treatment in 16 patients.

Feinberg and Feinberg[69] used prednisone in a number of allergic conditions, which included atopic dermatitis and chronic urticaria. Six patients with atopic dermatitis obtained improvement and there were no failures in this small series. Most patients obtained improvement from prednisone in doses of about one-fifth as large as those required with cortisone, and side effects included gastric complaints, euphoria, increased appetite, and over-stimulation. The initial dose of prednisone was 20 to 30 mg per day in most cases and the maintenance dose was between 10 and 20 mg daily. When patients were controlled with 10 mg daily it was noted that the drug could be discontinued without recurrence of the dermatitis.

Siegel and others[213] used prednisone in the treatment of 16 allergic children suffering either from asthma or atopic eczema. The ages ranged from 7 months to 11 years. Doses of 15 to 30 mg of prednisone were given for suppression of symptoms and 5 to 15 mg for maintenance. The only significant complications were definite evidence of moon facies and evidence of some sodium and water retention. While the preparation is effective it is suggested that further studies are necessary to determine whether complications may occur with long-continued therapy.

Rein and Bodian[186] treated a total of 212 patients having a variety of dermatoses with prednisone. Atopic dermatitis, contact dermatitis and seborrheic dermatitis comprised the greatest number in this series. Prednisone was taken in three or four divided doses. The initial suppressive dose was usually 40 mg per day, and this dose was then reduced to maintenance levels as rapidly as the clinical response warranted. The authors were favorably impressed with the therapeutic efficacy of prednisone which seemed to be four to five times more potent than hydrocortisone or cortisone. Maintenance doses ranged from 40 to 15 mg per day.

Preston and Flatt[169] used intravenous hydrocortisone hemisuccinate

and prednisolone hemisuccinate, preferring the latter in such conditions as drug eruptions, senile pruritus, acute contact dermatitis and generalized neurodermatitis, in which they noted a rapid response to these agents. Oral medication with steroids was then continued. This is a short preliminary report on the use of these agents in acute, severe dermatological conditions.

Scott and Kalz[206] made studies with radioactive hydrocortisone containing carbon 14 mixed with 1 per cent stable hydrocortisone ointment. This was applied under various conditions to the skin of normal human volunteers, to hyperkeratotic skin and to the skin of patients treated with ultraviolet and grenz irradiation. Biopsies and radioautographs were employed throughout the study. Radioactive material was visualized in the epidermis of normal skin after one hour. It was concentrated in the basal layer after two hours and in the cutis around the blood vessels after six hours. The material had disappeared entirely after sixteen hours. On hyperkeratotic skin the penetration was delayed. There were changes noted in irradiated skin which pointed to a more rapid penetration of the tagged hormone in the early erythema stage. There was no change, however, in the stage of late irradiation erythema. Penetration from hair follicles was equal to that of penetration from the remainder of the epidermis.

Atkinson and others[6] studied the effect on human skin of intradermally injected hydrocortisone. The injections were made into one or more skin sites of normal human subjects, using 0.1 to 0.2 ml, and this was followed by biopsy thirty minutes to seventy-two hours after injection. Local tissue damage was noted but inflammation was inhibited by the drug.

Kalz and Scott[112] tested 264 human volunteers with various hydrocortisone ointment bases. The main types of dermatoses studied included atopic dermatitis, seborrheic dermatitis and contact dermatitis. Precise formulas for the various ointment bases are recorded. As a general rule, the thinner the skin the more suitable are the greasy bases; in areas such as groin, axillae and antecubital fossa where there is increased perspiration, the drier bases produced the best results. The atopic patient proved to be the most difficult to satisfy, while the patient with contact dermatitis accepted almost all bases without trouble. Success with hydrocortisone preparations depends not so much on the penetration of hydrocortisone but rather on the compatability of the base with the skin disease and its different locations. Of four relatively poor bases, petrolatum provoked the largest number of complaints.

Loveman and Fliegelman[139] reported a systemic cutaneous allergic reaction from sodium carboxymethyl cellulose, which is a suspension vehicle for hydrocortisone (Merck). A white woman, aged 47, was given an injection of 0.2 cc of this material into and beneath the synovial cyst of the right fourth finger. After each injection except the first, the patient experienced an extensive hemorrhagic eruption. The eruption was reproduced with carboxymethyl cellulose, an ingredient of the vehicular fluid and while there were no local reactions to the intradermal injections, 0.3 cc injected subcutaneously reproduced the purpuric eruption. Prior to and during the cutaneous reactions, complete blood studies were essentially normal.

Rodnan and others[191] gave prednisone orally to 6 patients with progressive diffuse systemic scleroderma. Twenty to thirty milligrams of the drug in divided doses was given daily for periods up to four and

one-half months. Improvement in the skin and in the involved viscera including lungs and gastrointestinal tract was noted in all patients. The sedimentation rate was reduced and the C-reactive protein, when present before treatment, disappeared. Undesirable side effects of prednisone were minimal.

Salomon and others[198] treated 5 patients with systemic sarcoidosis using ACTH or cortisone. Improvement was noted in all patients. The lesions of the skin, peripheral lymph nodes, parotid gland and eyes were most favorably affected. These lesions regressed early in the course of treatment with no significant residuals. Visceral lesions showed less objective change but subjective improvement was noted especially in regard to dyspnea, cough and general well-being. There was no evidence that the basic, natural course of the disease was altered in any profound manner. Pulmonary changes of sarcoidosis responded more slowly to adrenocorticosteroid therapy than did skin and other visceral lesions.

Steinberg and Roodenburg[220] treated 6 patients with disseminated lupus erythematosus and 3 with periarteritis nodosa using meticorten. Improvement was obtained in 8 patients. One patient with periarteritis nodosa died and it was thought that treatment with meticorten had not been started sufficiently early. It was of interest that the lupus erythematosus phenomenon persisted in the bone marrow and peripheral blood in spite of effective control. All patients are on maintenance therapy.

Larochelle and Julien[125] reported the case of a 66-year-old-man with severe periarteritis nodosa and a background of asthma for many years. Purpura, which is commonly associated with periarteritis nodosa, also was present. He improved with the intravenous use of corticotropin and oral hydrocortone. Eosinophilia dropped from 44 to 7 per cent. A recurrence which appeared four months later was treated in a similar manner and once again the eosinophilia dropped from 54 to 13 per cent in ten days.

Foxworthy and others[74] gave adrenocorticotropin and cortisone to 10 patients with Reiter's syndrome. Six patients had the classic triad of urethritis, conjunctivitis and migratory polyarthritis. While not curative, corticotropin and cortisone are the most valuable agents now available to relieve pain, increase the patient's appetite, and prevent the excessive weight loss, muscle atrophy, and debility usually seen in patients with the severe form of Reiter's syndrome.

Cohen[46] reported the case of a 10-year-old-girl who was hospitalized because of Schonlein-Henoch purpura and severe renal involvement. Cortisone had no effect, but prednisolone produced a remission. Evidence of renal impairment, however, persisted.

Blodgett, Burgin and others[19] studied the results of prolonged use of cortisone in a number of dissimilar clinical entities including allergic disorders. It was found that cortisone usually slowed the rate of statural growth and skeletal maturation within one to two weeks after treatment was begun. Of significance, however, was the fact that a compensatory spurt in growth resulted in most cases when the drug was eliminated or even reduced. This study seems to answer the question of permanent growth retardation which was first brought up with regard to the use of cortisone in children.

Fitzgerald and Irvine[73] found that in most patients suffering from serum sickness resulting from antitetanus serum or penicillin, improvement could be quickly obtained by the administration of 300 to 500 mg

of cortisone given orally or a total dose of 25 units of corticotropin given intravenously over a period of eight to ten hours. The earlier the treatment was started, the more easily symptoms were suppressed. Patients with allergic reactions to penicillin did not respond as quickly as did patients with antitetanus serum reactions, and they required a longer period of therapy. Recurrences may appear after therapy has been discontinued but these may be controlled by further intermittent therapy. There were no unfavorable reactions to the administration of either cortisone or corticotropin in any of the 55 patients studied.

Olansky and others[137] reported the case of a 42-year-old-woman with chronic lymphatic leukemia who was given a course of smallpox vaccination for recurrent herpes simplex of the lip. A primary reaction was obtained and during the next few weeks generalized vaccinia developed. She had been treated with triethylene melamine and cortisone using intermittent dosage. In spite of treatment with antibiotics, gamma globulin and other supportive measures including blood transfusions, the patient died forty-nine days after the initial vaccination. As is well known, there have been a number of deaths in children who have contracted varicella while receiving cortisone therapy for other conditions.

MISCELLANEOUS ALLERGIES AND BRIEF REVIEWS

Kesten[115] gave a brief but comprehensive report on the effect of sunlight on the skin and notes that sun's rays of less than 2,900 Å do not penetrate the atmosphere and that the biological action of wave lengths longer than 14,000 Å in sunlight has not been sufficiently explored. Ultraviolet rays fall between 2,900 and 3,900 Å, visible light between 3,900 and 7,700 Å and near infra-red between 7,700 and 14,000 Å. The erythema caused by the sun's rays is produced by well-defined wave lengths of the ultraviolet rays between 2,800 and 3,132 Å, the so-called sunburn range. Allergic eruptions caused by sunlight are not uncommon. Intense cutaneous reactions may follow exposures that would cause no perceptible reaction in normal skin. Urticaria and various dermatoses of an inflammatory nature sometimes associated with purpura may appear after minimal exposure. Lesions resembling lupus erythematosus may be seen. Some chemicals can photosensitize the skin to long wave ultraviolet and to visible rays. There are rare reports of photosensitivity after oral ingestion of para-aminobenzoates, salicylates, chlortetracycline, stilbamidine, phenylbutazone and antihistaminics, and also more frequent, recent reports of sensitivity after chlorpromazine therapy. The ingestion of antimalarial drugs such as quinine, quinacrine hydrochloride, chloroquine phosphate and pamaquine has effectively controlled a number of eruptions caused or precipitated by sunlight. Kesten also mentions sunscreen barriers in this report.

In response to a query[178] regarding allergy to sunlight it was noted that the simplest way to prevent this reaction is to use a screening agent. One of the best of such chemicals is p-aminobenzoic acid or its ester. Concentrations used are from 1 to 10 per cent and preparations called Tartan or Skolex are suitable for use as sunscreen barriers. Recent developments have indicated that certain chemicals taken internally, notably the antimalarial drugs, have an effective sunscreen action.

In discussing responses to physical agents, Baer[9] noted that human skin can be made hypersensitive to light by intracutaneous or systemic administration of rose bengal and certain other agents. This hyper-

sensitivity is not an altered reactivity of the skin but is based on the photodynamic action of rose bengal. The urticarial lesion cannot be differentiated from any other clinically produced urticaria. It is postulated that the physical agent releases a metabolite normally inherent in the skin. In the allergic individual, however, the metabolite acts as an allergen. Further evidence of an allergic causal mechanism is the finding of passive transfer antibodies in some cases of cold and light sensitivity; the occurrence of a shorter reaction time; the clinical resemblance of the morphe of urticaria due to light (4,000-5,000 Å passive transfer antibodies absent) and lesions due to light (less than 3,700 Å specific antibodies present); and anaphylactoid reactions associated with cold urticaria.

Allington[3] has reviewed the eczematous and polymorphous hypersensitivities to light. Polymorphous light-sensitivities are a poorly defined group of eruptions. The types seen include: (1) erythema with or without edema; (2) erythema multiforme; (3) eczema; (4) papular urticaria or prurigo, and (5) chronic inflammatory plaquelike dermatitis. There is much overlapping and combining of these groups. Some believe that many polymorphous light eruptions are subclinical manifestations of systemic lupus erythematosus. Prurigo aestivalis and vesiculobullous types of solar dermatitis now described as hydroa aestivale or hydroa vacciniforme may properly fall in the family of light sensitive dermatosis. The finding of porphyria in any patient with light sensitivity removes the case from this simple classification. Rare cases of congenital or erythropoietic porphyria and the cutanea tarda type of hepatic porphyria present cutaneous changes described in polymorphous light sensitivity. All patients in this category should have urine tested for porphyrins, preferably during an acute attack. Evidence of an allergic mechanism is presented in some cases of polymorphous light sensitivity.

Epstein[65] discussed solar urticaria (urticaria photogenica). This condition may begin suddenly at any time of life and may last for many years. Females predominate three to one. Experimental lesions are easily produced by the application of light to the skin. The wheal which results is confined to the exposed site and never has pseudopods. All parts of the visual spectrum, as well as the ultraviolet and the infrared, have been found to cause urticaria solaris. Most patients are sensitive to radiation of less than 3,700 Angstrom units. Evidence for the allergic nature of urticaria solaris is presented. There is an excellent summary of the theoretical considerations of this problem. Treatment of these patients includes the use of Pyribenzamine, the antimalarials, and gradual desensitizing exposures to ultraviolet light. Nonspecific measures which have been advocated include the eradication of focal infections and treatment with female or male hormones. Para-aminobenzoic acid protects against ultraviolet light and physical barrier agents such as titanium dioxide or zinc oxide protect against longer ultraviolet rays and visible light.

Jillson[108] discussed heat hypersensitivity. The reactions seen are generalized (cholinogenic) urticaria produced by heat, exercise and emotional stress; and a local (noncholinogenic) urticaria produced by heat alone. The latter form is rare. Cholinogenic wheals are small (1 to 2 mm in size) and are surrounded by a large axone reflex flare. On the body, diffuse erythema may occur without whealing; skin lesions or itching never occur on the palms or the soles and rarely in the axillae. In about 50 per cent of these patients systemic reactions due

to endogenous acetylcholine may occur and these are manifested by abdominal cramps, diarrhea, faintness, sweating, salivation and headaches. The basic work of Grant (1936) is reviewed, and the newer confirmatory evidence using combinations of cholinergic drugs is presented. Intradermal testing with Mecholyl, 0.01 mg dissolved in 0.05 cc physiologic saline, is used. Treatment with various anticholinergic drugs, tertiary amines (Syntropan) as well as the quaternary amines (Banthine and Prantal) has not been consistently effective. Antihistamines are partially dependable. The treatment of choice is to rest and cool the body. "Hyposensitization" to heat is beneficial in some cases.

Lorincz[137] discussed hypersensitivity to trauma with evidence of increased or abnormal reactivity of the skin to such varied stimuli as scratching, stroking, pressure and so forth. Dermographism of the red or white type may be seen. Mechanically induced urticaria is seen in urticaria pigmentosa and at the sites of old insect bites. Other examples are blister formation in epidermolysis bullosa and some porphyrias; lichenification in atopic dermatitis, chronic contact eczema and lymphoblastomas; purpura; hyperkeratinization; hyperesthesia and epidermal fragility seen in infantile eczema. Urticarial dermographism appears in about the same frequency in acute and chronic urticaria as in the normal population. Passive transfer is possible in some patients with urticarial dermographia. In this condition as well as in lichenification the possibility exists that an allergy to some product arising in response to mechanical stimuli explains the way in which clinical symptoms are produced.

According to Griem and Rothman[80] the following types of cutaneous sensitivity to cold can be distinguished on the basis of clinical and serologic studies: (1) cryoglobulinemia; (2) syphilitic paroxysmal cold hemoglobinuria; (3) cold hemagglutination, and (4) essential cold urticaria. Cryoglobulins are present in kala-azar and in small amounts in subacute bacterial endocarditis. Other diseases also show this change to some extent: multiple myeloma; chronic lymphatic leukemia; rheumatoid arthritis and other serious systemic diseases. A simple screening test for cryoglobulins is performed by drawing venous blood into a syringe that has been warmed to 37° C. and allowing it to clot at 37° C. The serum is separated and is cooled to 5° C. Cryoglobulins precipitate as small, discrete, white particles that dissolve when the serum is rewarmed to 37° C. The cryoglobulins may precipitate at room temperature if they occur in high concentrations. Cold hemagglutination is a serologic reaction in which there is agglutination of homologous or heterologous erythrocytes at low temperatures, with complete reversal of the reaction upon rewarming. No complement is required for this reaction. Ischemia noted in this condition may result in cutaneous manifestations.

Irgang[104] reported a case of allergic cutaneous vasculitis manifested by a polymorphous eruption which histologically showed a uniform inflammatory process. The predominating finding was an arteriolitis confined principally to the vessels of the cutis. The case presented was that of a Negro woman aged 29 who complained of painful, tender swellings of the ankles and feet and of an eruption on the lower extremities of ten weeks' duration. This was accompanied by weakness, anorexia and polyarthralgia. After the diagnosis was established, the patient received 15 daily intramuscular injections of 600,000 units each of procaine penicillin without effect on the lesions. The eruption resolved gradually, and healing was complete about six months after its inception leaving

residual hyperpigmentation. There is general agreement regarding the pathogenesis of allergic cutaneous vasculitis, namely, hematogenous bacterial dissemination.

Rostenberg and Iverson[195] presented the case of a 49 year old white man who, after receiving penicillin, developed swelling and pain in the joints of the hands, elbows, knees and ankles, with the appearance of erythema multiforme of the skin. A biopsy from one of the skin lesions showed a necrotizing vasculitis. Eosinophilia was not mentioned in the protocols. In discussion it was noted that necrotizing vasculitis was originally called periarteritis nodosa. In a recent survey, two-thirds of the reported cases of periarteritis nodosa failed to reveal any clinical evidence of sensitization. A further classification includes: cutaneous allergic vasculitis; systemic allergic vasculitis; granulomatous allergic vasculitis, and periarteritis nodosa. Cutaneous vasculitis is benign and usually there is a history of allergy to drugs. The patient usually presents persistent urticaria-like papules. Sometimes there are lesions suggesting Schoenlein's purpura or papulonecrotic tuberculid. Systemic allergic vasculitis is the most serious of this group and usually appears after sensitization to sulfonamides, penicillin, thiouracil, thiourea, iodides and dilantin. The difference between systemic allergic vasculitis and periarteritis nodosa is the absence of any clinical evidence of sensitization in the latter condition. In systemic allergic vasculitis, arterioles and venules of the collagen type are affected whereas in periarteritis nodosa, small and medium sized arteries of the muscular type are involved. Granulomatous allergic vasculitis is a widespread condition showing cutaneous and systemic manifestations, but it is not as severe as systemic allergic vasculitis. Gougerot's nodular allergides consists of purpuric macules, small subcutaneous dermal nodules and vascular lesions.

McCombs[148] and others studied 30 patients in whom, during life, a diagnosis of allergic vasculitis was established by skin or muscle biopsy. Clinical observation and postmortem studies in some cases failed to establish a diagnosis such as lupus erythematosus disseminatus or periarteritis nodosa. Eighteen of the 30 patients at one time or another had contact dermatitis with id reaction; urticaria with angioedema; vascular purpura; erythema nodosum, or dermatomyositis. Systemic symptoms included arthralgias, edema, purpura, fever, weight loss, subcutaneous nodules, pneumonitis, dermatitis, muscle tenderness and weakness, urticaria, neuritis, gastrointestinal bleeding and renal failure. With patients in whom antibiotics, infective agents or malignant tumors seem to serve as antigens, the vascular damage could then be said to result from antigen-antibody reaction fixed in the vessel wall. Prognosis for recovery is good in all cases except those with irreversible renal disease.

Gitlin and others[82] described the multiple serum protein deficiencies in congenital and acquired agammaglobulinemia. There is a physiologic or transient form that occurs in infants; a congenital form occurring only in males and an acquired form occurring in both sexes which may have its onset either in adolescence or adulthood. In studying the sera of these patients it was noted that in addition to gamma globulin, at least two other plasma proteins were either markedly diminished or entirely missing in the congenital and acquired forms of the disease. It seems that the absence of plasma cells in these patients causes the failure of synthesis of gamma globulin.

Mazzitello and Good[147] discussed the metabolic disorder agammaglobulinemia which was first described by Bruten in 1952. The absence

of gamma globulin was recorded in the electrophoretic pattern of a pediatric patient who showed repeated bacterial infection. The congenital form of this disorder occurs only in male children and is transmitted as a mendelian sex-linked recessive trait. The acquired form occurs in both male and female adults who usually have had a history of general good health in the past. Characteristics of the syndrome include absence of isohemagglutinins, failure of plasma cell formation, lack of antibodies in the blood and tissues, failure of immunologic response to antigenic stimulation, and the clinical appearance of repeated bacterial infections. The plasma cell may be responsible for the formation of both antibody and gamma globulin. In suspected cases 0.6 cc of standard gamma globulin preparation per kilogram of body weight is given at four-week intervals. Capillary bleeding and chronic, recurrent, purpuric states are associated with various abnormal serum proteins. Symon and others[228] classified these abnormal globulins as follows: macroglobulins, cryoglobulins, and hyperglobulins. In one patient with hyperglobulins this disorder was associated with disseminated reticulum cell sarcoma.

Sandberg and others[200] studied the effects of intravenous administration of immune globulin, comparing it to albumin. This has not been previously investigated because of its alleged toxicity. Over 120 infusions of large doses (up to 100 gm per injection) of immune globulin were given to 15 subjects. Commercially available "poliomyelitis immune globulin" was diluted with 0.25 to 1.0 L. of isotonic saline or 5 per cent glucose and given intravenously over periods of 0.3 to 6 hours. Sudden systemic changes consisting of peculiar collapse without changes in blood pressure, electrocardiogram or pulse occurred but the patients recovered quickly and later received large doses without such reactions. Nevertheless this study indicates that fairly large doses of gamma globulin can be given as required, as in cases of agammaglobulinemia.

Wolf[252] described the case of a 70-year-old-man with an eruption on the hands, feet and nose of about twelve years' duration. The process continued throughout the entire winter and improved with the appearance of warm weather. It was thought that the patient was suffering from cryoglobulinemia. The commonest manifestations of this disorder are purpuric lesions or mottling of the skin of the extremities and intolerance to heat or cold. Cryoglobulin, which seems to be a gamma globulin, is present in the blood of a significant percentage of people without symptoms. In order to cause symptoms, 20 mg or more per 100 cc should be present in the blood. Cryoglobulinemia may be found as an idiopathic condition. It may be found in bacterial endocarditis, bronchiectasis, lymphosarcoma, Hodgkin's disease and kala-azar. For this patient, preliminary studies showed a definite precipitation at 40° C. and considerable precipitation at the end of twenty-four hours.

Campbell and others[33] presented the case of a 29-year-old-housewife who was admitted with a recurrent hemorrhagic disorder of eleven years' duration, manifested by recurrent episodes of menorrhagia and spontaneous ecchymoses. These symptoms together with migratory polyarthritis and the subsequent finding of L.E. cells led to a diagnosis of disseminated lupus erythematosus. The clotting times of blood in glass and silicone and of recalcified plasma were prolonged. In this patient there was no deficiency of the coagulation factor but an anticoagulant existed which disappeared during steroid therapy. The mechanism of the marked prolongation of coagulation is described.

In studying the L.E. cell phenomenon of systemic lupus erythematosus, Kurnick[121] believes that the abnormal factor in the gamma globulin of the patient alters the cell membrane, admitting a serum proteolytic enzyme into the cell which destroys the protein inhibitor of desoxyribonuclease (DNase). The addition of the inhibitor of DNase *in vitro* to the combined lupus erythematosus serum-normal leukocyte system, inhibits the L.E. cell phenomenon. Sixteen patients were given homologous fresh whole blood of leukocyte homogenates intramuscularly for treatment. Skin lesions cleared and arthralgias, myalgias and fever subsided within one to two months. Steroids were successfully discontinued in almost all cases.

A symptom complex resembling lupus erythematosus of the disseminated type has previously been observed in 8 to 15 per cent of patients with hypertension who have been treated for a period of time with large doses of Apresoline (hydralazine hydrochloride). Comens[49] was able to reproduce this syndrome in dogs who developed weakness, weight loss, anemia and changed electrophoretic patterns when given Apresoline in a similar dosage to that used in humans. Pathologic study showed that changes in the kidneys were consistent with those found in disseminated lupus erythematosus.

Jillson[109] showed the relationship between various allergic dermatoses produced by pathogenic and saprophytic fungi. He described the occurrence and appearance of dermatophytids, disseminated papular lesions, vesiculopapular dermatophytid of the hands, erysipelas-like dermatophytid, migrating thrombophlebitis and a miscellaneous group of ids which includes urticaria, erythema multiforme, erythema nodosum and erythema annulare centrifugum. It is important to remember that in testing with trichophytin, three types of reactions have been noted: wheal, papule and plaque. In addition, a four to six hour edematous reaction may occur. A positive immediate wheal signifies past, present or future sensitization, and may not be related to the present condition. Furthermore, a positive wheal may utilize the antigen completely and therefore no antigenic extract remains to produce the papule at forty-eight hours. A positive wheal without subsequent delayed papular reaction may be associated within twelve to forty-eight hours with a flare of the original dermatitis or precipitate a new lesion. If a papule is noted with a concomitant flare of the dermatitis, this represents the strongest aid in diagnosis. The one week eczematous reaction should be looked for. It is invariably associated with a flare of the dermatitis and is certainly of etiologic significance. Patch test reactions can be used in detecting sensitivity to molds as well as to defatted pollen proteins of grass, ragweed, feathers, and dander. In treatment, all effort should be made to avoid molds by following dust elimination procedures. Desensitization can be accomplished by means of extremely dilute antigens given in relatively fixed amounts, which are usually self-administered. Desensitization can be accomplished if it is suspected that such molds as Alternaria, Cladosporium, Aspergillus, Penicillium, Pullularia and Mycelia sterila may be involved. Dust may be added to the mold mixture in concentrations of one to one million, and molds 1/10 protein nitrogen unit per cubic centimeter.

Cohen[47] reported the case of a 59-year-old-housewife with a ten-year history of recurrent dermatitis of the anogenital area with lesions on the buttocks, thighs and flexor surfaces of the elbows and knees. Scrapings of the scales in the anogenital area proved to be Trichophyton gypseum

on culture. An intracutaneous test with trichophytin showed a positive reaction of an immediate wheal. There was no delayed or forty-eight hour reaction. When hydrocortisone was given, the distal lesions subsided rapidly and the crural lesions responded to local measures. The presence of circulating reagins to Trichophyton could not definitely be proved. This case is unusual because immediate wheals to Trichophyton extract are usually shown with Trichophyton purpureum; however, they have been observed in the course of Trichophyton desensitization. The significance of the urticarial reaction is not clear, and it has never been determined whether these test responses and findings of reagins are more common in atopic than in nonatopic subjects.

Rogachefsky and others[192] have been studying massive exposures of human beings to pathogenic fungi. However, despite overwhelming exposures, the investigators were unable to produce clinical fungous disease of the feet in subjects with mycologically and clinically healthy feet. Fungi were temporarily established on the feet of some of the volunteers, as suggested by positive microscopic fungous examinations in 56 per cent of previously fungous-free feet. To continue this study, numerous tests were made with Trichophyton extract 0.01 ml injected intracutaneously in the lower flexor aspect of the right forearm. Of 63 subjects who had had negative immediate urticarial reaction and who were deliberately exposed to dermatophytes, 8 developed a positive immediate reaction in the repeat tests. Of the subjects, 40.4 per cent developed a positive delayed reaction in the repeat tests who were previously negative on this type of reaction. The results of these experiments suggested that massive deliberate fungus exposures were capable of producing or reawakening trichophytin sensitivity in many of the volunteers. Various mechanisms are discussed and in this connection it should be remembered that Cole and Favor (1955) have shown that the urticarial and anaphylactic sensitivity to tuberculin, on the one hand, and delayed sensitivity, on the other, are elicited by different fractions in tuberculin and are mediated by different antibodies contained in the plasma fractions of various guinea pigs.

Popoff and Wheelock[168] discussed Weber-Christian disease. This is manifested as nodular, nonsuppurative, inflammatory lesions in the subcutaneous fat usually of the lower extremities, but may also appear on the abdomen and breasts of women. With many patients, outbreaks of nodules and especially recurrences followed an upper respiratory infection. A large number of eosinophils found within the nonsuppurative lesions suggest an allergic disorder. Patients may have an inherited tendency to become sensitized by stimuli, which may be bacterial, viral or chemical in origin. The reviewer noted that the most successful treatment was an antibiotic given simultaneously with adequate doses of corticotropin. Although this is not curative, the combination of these two agents is effective in controlling the disorder.

The question of tuberculin reaction and its conversion from positive to negative in later life brought the following response in Queries and Minor Notes.[172] The old belief regarding tuberculin reactions that "once a reactor, always a reactor" has been disproved by observation. Accumulated evidence has shown that tuberculoprotein must be present to sustain sensitivity of tissues to tuberculin. If the bacilli die, sensitivity of tissues to tuberculin wanes and disappears. Human beings and animals can be made reactors to tuberculin by introducing sufficient numbers of dead tubercle bacilli. However, such sensitivity soon disappears

unless it is sustained by periodic administration of dead bacilli. A characteristic tuberculin reaction may be regarded as indicating the presence of live tubercle bacilli. Before the use of antimicrobial drugs, it was observed that some persons reverted from reactors to nonreactors to tuberculin, including those late in life. No extensive study has been made to determine how often this occurs from natural infection. Administration of antimicrobial drugs to persons recently infected, and therefore tuberculin reactors, has resulted in their reversion to nonreactors after eight months or longer of drug administration. Whether this is due to destruction of the tubercle bacilli or simply to suppression, has not been determined.

Israel and Sones[106] used test material prepared from the cervical lymph nodes of a patient with sarcoidosis. They performed 114 tests in 81 patients, using the Kveim reaction. Of this group, 28 patients had sarcoidosis and 33 had tuberculosis. Twenty additional controls were used. Because a significant group of patients in the control and tuberculosis series showed positive reactions, it is believed that the Kveim reaction cannot be relied upon in its present form to establish the diagnosis of sarcoidosis. The test does not appear to be a specific allergic response, nor is it a characteristic tissue reaction of patients with sarcoidosis to nonspecific irritants. Tuberculosis, histoplasmosis and berylliosis are diseases which particularly simulate sarcoidosis and must be ruled out by standard studies.

Wysham and others[253] studied an epidemic of staphylococcal infections in which 46 per cent of 117 infants developed clinical staphylococcal infections of the skin. The source of the staphylococci causing the epidemic was studied by taking daily cultures from the infants in the nursery, from their mothers, from fomites, and from the air in the nursery. Repeated cultures were taken from the noses and hands of nursery personnel. The majority of infections were caused by a single strain of staphylococcus, termed the epidemic strain. It was found to be resistant to penicillin, Streptomycin and Tetracycline. The mothers were not the source of the epidemic strain of staphylococci. Infants with subclinical staphylococcus infections disseminated large numbers of organisms into the nursey environment and it was felt that the transmission was mostly from infant to infant, probably through the air. The nurserv personnel were found to be of relatively little importance in this study as sources or as transmitters of the strain of epidemic staphylococci.

Stubenrauch and others[225] found that a combined antibiotic ointment was effective in 113 of 192 cases of primary and secondary pyoderma. The material (Biotres) contained a combination of zinc bacitracin 200 units, neomycin base 3 mg, polymyxin B 4,000 units, and benzalkonium chloride 5 mg per gram of special hydrocarbon base.

Rostenberg and others[196] have previously shown that in most cases of lymphoblastomas a negative reaction to the tuberculin test could be expected. The next study was an attempt to sensitize these patients to a known agent such as 2:4 dinitrochlorobenzene. Sensitizing potentials of this substance have been extensively studied by various workers over many years. An eczematous sensitization developed in only one of the 31 patients with lymphoblastoma treated in this manner. A control group of patients with other ailments was used and 3 of these patients became sensitized. Ten patients with either lymphoma or leukemia were passively sensitized with known human sera containing antibodies against ragweed, and in one case with guinea pig serum. Positive passive trans-

fer reactions were noted in each case when the sites were challenged with the specific antigen. There is a discussion of the theoretical reason for the impaired ability of patients in the lymphoma group to develop allergic eczematous sensitization.

Blatt[18] has reviewed some of the current evidence for the existence of bacterial allergy and dermatology. The role of bacteria in dermatologic conditions is discussed in Loewenthal's book, The Eczemas (edited by L. J. A. Loewenthal, Edinburgh and London, E. and A. Livingston, 1954). It was shown that filtrates of broth cultures of Staphylococcus aureus provoked eczematous reactions. This was observed frequently in eczematous patients and infrequently in normal individuals. It was believed that these reactions were allergic and not toxic. In patients with eczema, there seems to be a specificity in the sensitization to the staphylococcus, according to Storck. Eczema-producing strains differ serologically from pathogenic strains. The chief characteristic is the delayed response. Others have shown that in patients with atopic dermatitis, acute upper respiratory or focal infections may aggravate the dermatitis and that skin tests with bacterial antigens are useful in establishing the importance of such infections in the patient. Sulzberger and Baer (Yearbook of Dermatology and Syphilology, 1946) while agreeing that these reactions exist, believe that this is not an immunologic reaction of specific bacterial-viral hypersensitivity. Glaser[83] stated that among children, foci of infection are rarely the cause, but that urticaria secondary to an infection is fairly frequent.

In a subsection of an extensive review on allergy to bacterial products, Baird[12] summarized some of the important contributions of various authors who have shown the relationship of bacterial products and certain dermatoses. These dermatoses may range from simple eczematous dermatoses to bullous eruptions and pustular bacterid of Andrews. The relationship of urticaria, erythema nodosum, eczema and psoriasis to bacterial sensitization is well described in a number of significant references in the literature. The reviewer notes that the position of bacterial sensitization in the field of dermatology is still highly controversial, but that many favorable reports by dermatologists are now regularly appearing in the literature. It would seem that further progress in this field is urgently needed. In recent years, due to advances in therapy, antibiotics, steroids and antihistaminics, the dermatologist no longer sees simple cases. Many of the dermatologic problems now seen may very well be solved by advances in our knowledge of sensitization to bacteria and fungi.

Lincoln[133] reported the case of a 23-year-old-white housewife who had a background of asthma and who developed severe systemic disease pointing to disseminated allergic granulomatosis. Small, dark, papular to nodular skin lesions were seen over the dorsa of both hands and extensors of elbows and knees. There were areas of deep pigmentation and shallow scars at the sites of healed skin lesions. Aside from the skin findings, the patient presented all the cardinal signs and symptoms of this disorder. She had a three year history of asthma with the eventual development of a bilateral lower lobe pneumonic infiltration and cystic bone lesions of the right sixth and seventh and left seventh ribs. This was accompanied by pathological fractures, cough, fever, loss of appetite, pronounced weight loss, weakness, abdominal cramping with bloody diarrhea, splenomegaly, intermittent urinary abnormalities and a decided

eosinophilia ranging as high as 51 per cent. The pathology of the cutaneous disease is presented.

Chase and others[41] noted peculiar granulomatous lesions similar to sarcoidosis in guinea pigs sensitized by methods in which killed tubercle bacilli were used as adjuvants. These lesions are located in the loose connective tissue between the subcutis and muscularis and resemble sarcoidosis in appearance. The author noted that this type of sensitization may be related to the various eosinophilic granulomas seen in sensitized individuals who are developing evidences of allergic vasculitis. These studies are continuing.

Allergic granulomatosis has been reported more and more frequently by dermatologists. Brunsting and Eyster[25] reported the case of a 28-year-old white woman who had an eruption shortly after her child was vaccinated. Peculiar, crusted, varioliform lesions involved the arms, face and soles. The vesicles were mucous-filled, did not rupture, and as they progressed they became organized into a granulomatous type of lesion. During this time she was febrile and acutely ill. Investigation of her background revealed marked allergic phenomena, such as asthma and previous eruptions due to chocolates, oranges and other foods. The lesions were controlled by cortisone therapy. She was referred to an allergist and was found to be extremely sensitive to dust, pollen and a number of foods. Flare-ups could very easily be produced with pollen extracts. Allergic granulomatosis occurs in persons with allergic backgrounds and is characterized by fever, leukocytosis, eosinophilia, and occasionally pulmonary infiltration similar to that seen in Loeffler's pneumonia. Systemic manifestations may be present. Cutaneous manifestations may resemble erythema multiforme, hemorrhagic lesions or subcutaneous and cutaneous nodules. The lesions tend to occur in crops and may persist for a week or even months. The lesions heal without scarring except when necrosis occurs. Histologically, the cutaneous as well as the visceral lesions of allergic granulomatosis are characterized by granulomatous inflammation with marked eosinophilia, although there may be necrosis as well as the presence of histiocytes and giant cells. It is sometimes difficult to differentiate allergic granulomatosis from periarteritis nodosa.

Rubin and others[197] reported 4 cases of a new and unusual type of eruption in the axillas caused by deodorant and antiperspirant preparations. This eruption is characterized by diffuse erythema and severe pruritus. Microscopically, a tuberculoid type of reaction is found. The exact agent responsible for this change caused by the use of deodorant sticks has not been determined. Pinkus and Botvinick[167] presented the case of a 22 year-old-woman whose chief complaint was severe pruritic eruption on both axillas. In the discussion it was noted that similar lesions have been seen by a number of dermatologists in patients who have used stick deodorants and that these eruptions become fixed. From the discussion it would appear that zirconium may be a causative factor. The tissue reaction is similar to sarcoidosis and beryllium granuloma, and may well be simply a foreign body reaction. In a similar presentation, Lewe[132] found an itching eruption of both axillas in a Mexican woman aged 45. This occurred after the use of Stopette liquid and Stopette stick deodorant. It was noted in discussion that the zirconium used in poison ivy and poison oak preparations is not the same as that used in stick deodorants. Three cases of granuloma of the axilla were presented by Cormia and others,[50] and it was the consensus that zirconium may possibly

be responsible for this unusual new type of dermatitis caused by the use of deodorant stick. The chemistry of the subject was reviewed by Sheard who had personal knowledge of poison ivy preparations with zirconium. It was emphasized that in poison ivy preparations only insoluble zirconium salts that do not penetrate the epidermis to any degree are used. Their function is to absorb the toxic chemical, the ivy oleoresins, selectively. The use of zirconium in stick deodorant was said to have started when a man packing this preparation who had a notorious body odor suddenly began to smell sweetly. Tests were performed on volunteers and it was decided that zirconium was effective in combating body odor. The present stick deodorant contains 70 per cent alcohol, 10 per cent water or glycerin and another 7 per cent stearic acid soap. In addition, small amounts of perfume and usually hexachlorophene are added, and the balance is made up of about 6.5 to 8 per cent of sodium zirconium lactate. The stick contains soluble zirconium salt. A number of deodorant antiperspirant sticks on the market contain zirconium.

Prickman and Lofgren[170] have devised an emergency set to combat the anaphylaxis sometimes seen after use of urographic solutions, wasp, yellow jacket or bee stings, or drug reactions. The suggestion is made that a substance for which there is even a questionable history of hypersensitivity should never be given. The anaphylactic set contains the following items: two 1-cc ampules of 1:1,000 solution of epinephrine, two 2-cc syringes, two hypodermic needles, two long needles (1 inch and 4 inches long), two ampules of aminophylline (3¾ grains each), one 1,000-cc bottle of 5 per cent solution of dextrose in distilled water, one set of intravenous apparatus, one 10-cc ampule of diphenhydramine hydrochloride (Benadryl) containing 10 mg per cubic centimeter, one bottle of hydrocortisone (dilution to 2 cc gives 50 mg per 1 cc), one ampule of sterile water, one scalpel, one hemostat, one ampule of absorbable surgical suture (catgut) with needle, alcohol, gauze sponges, a swab tongue blade and one 20-cc syringe. Anyone who has attempted to assemble even a part of the above group of items during the stress of caring for a patient with an anaphylactic reaction, which can be fatal, will appreciate having these tools ready beforehand for emergency use.

Every allergist of experience will ultimately be called upon to treat patients who have either mild skin reactions or more severe anaphylactic reactions from insect bites. There has been some confusion, however, about the cross sensitivities with extracts of various insects in the Hymenoptera class. Previous reports had indicated that clinical immunity can be achieved in a limited number of cases by hyposensitization with whole body extract as well as by the accidental or planned intermittent stings of live insects. Loveless and Fackler[138] have made an important contribution to the subject of insect allergy by carefully planned clinical experiments supported by laboratory data. Venom was removed from the extirpated sacs of live wasps and used for the first time in the diagnosis and immunization of wasp allergic individuals. Levels of response were tested by means of concurrent tests of the skin and eyes, as well as a three minute sting with a live worker insect. Responses of immunized patients to deliberate insect stings were similar to those of the control group. Experiments indicated that five of the Hymenoptera (yellow jacket, baldfaced hornet, paper wasp, honey bee and bumble bee) possess a common allergenic specificity, while the venom of each also contains a component which is peculiar to the particular insect. The honey bee seems to be more closely related to the three wasps

examined than is the bumble bee, and the three wasps have many common characteristics. Wasp venom was found to be a saisfactory immunizing agent, and it is of special interest that prolonged injection series were not necessary. The venom from as few as six sacs appeared to be sufficient for protection and could be administered during a single prolonged office visit without untoward effect. The intracutaneous injections were uniformly employed in immunization procedures. Overdose reactions were seen, and they are described in full.

Properdin is a naturally occurring serum protein, combining *in vitro* with certain high molecular weight polysaccharide complexes. Properdin is essential for certain viricidal, bactericidal and hemolytic properties of normal human serum. Low properdin levels have been observed following shock, radiation and experimental infection. Hinz and Murphy[96] observed that properdin levels in normal persons remain constant; they bear no relation to age, sex or leukocyte count, and are unaffected by "stress" and radiotherapy. Low properdin levels have been repeatedly observed in a patient with paroxysmal nocturnal hemoglobinuria. A study of properdin levels in patients with eczema and atopic dermatitis complicated by pyoderma would be of interest.

Delaney and others[56] studied properdin and its significance in immunology. A complex (pz) is formed when zymosan, a soluble residue obtained by treating fresh yeast with trypsin and alcohol, is added to human serum at certain temperatures. This residue unites with a particular factor of the serum named properdin (p). This combination has an inactivating effect on certain forms of complement. Properdin is high in animals that have a high natural immunity to bacteria and viruses. Human properdin is an euglobulin with a molecular weight of at least 8 times that of gamma globulin, and it has a bactericidal action. It may be involved in the thermo-labile factor of serums capable of inactivating some viruses. Properdin increases the resistance of animals to the secondary effects of radiation and to bacterial infection. The properdin system (properdin associated with complement in the presence of Mg + +) can cause hemolysis of certain abnormal erythrocytes, as is seen with nocturnal paroxysmal hemoglobinuria.

Humphrey and others[102] studied the release of histamine and serotonin from platelets by an antigen-antibody reaction *in vitro*. This was accomplished by the addition of an antigen to rabbit platelets suspended in heparinized plasma which contained specific antibodies. This was followed by release from the platelets of histamine and serotonin. Serotonin is of interest because the preparation when aerosolized produces bronchoconstriction in asthmatics. It was determined that neither fibrin nor thrombin was concerned in this release.

Favour[68] described the results obtained with a new anti-inflammatory agent, RO 2-5383/2, which is a pyrimidine derivative. Suppression of inflammation was seen in animals treated with this substance—25 mg per cent per kilogram of body weight twice daily. The anti-inflammatory effects were noted in skin lesions produced by: (1) a mild nonspecific irritant (autoclaved yeast particles); (2) a toxic, nonspecific irritant (turpentine); and (3) specific delayed-type allergy (tuberculin reactions). Control animals treated with cortisone-hemisuccinate—10 mg per cent per kilogram of body weight intramuscularly twice daily—showed a greater suppression of reactions. Local injection of either drug with test materials gave similar results. It was concluded that this agent is useful

for studying the pathogenesis of inflammation. It may prove effective in the treatment of inflammatory and allergic disorders.

Close and Kory[44] found a method of preventing the occurrence of cutaneous necrosis after the intravenous use of norepinephrine. Intense venospasm generally occurs when norepinephrine is infused into a vein. Using dogs as subjects, it was found that if the tissues were infiltrated with either regitine or priscoline in saline solutions with or without hyaluronidase, cutaneous necrosis was prevented. This observation strongly suggests that ischemia of the vein wall permits diffusion of norepinephrine into adjacent tissues. Prolonged tissue anoxia leads to slough.

Singleton and Little[214] made a follow-up study of 250 patients who had been given 1500 units of tetanus antitoxin. They recorded an 11.2 per cent reaction rate when tetanus antitoxin was given alone. In a similar group of 250, the reaction rate dropped to 7.2 per cent when Phenergan was given in addition to the tetanus antitoxin. Phenergan was continued, 25 mg each night for 7 doses after the initial injection of tetanus antitoxin. By Chi Square analysis, Phenergan does not appear to have much statistical significance in reducing reactions to tetanus antitoxin.

Godden and others[84] described 4 patients with a diagnosis of Hodgkin's disease who experienced attacks of severe pain promptly after drinking beer, wine of other alcoholic beverages. Each patient experienced relief from this symptom during remissions induced by nitrogen mustard or irradiation therapy. Intense, distressing and acute pain has its onset during the consumption of the beverage or at an interval reported as immediately or almost immediately after consumption. The amount of alcohol required to produce pain in sensitive patients is small, being variously reported as "one or 2 mouthfuls of beer, brandy or sherry." Alcoholic beverages did not produce any other effects of an allergic nature in the 15 reported cases in the literature. The pain is located in the regions of granulomatous deposits found in Hodgkin's disease. The mechanism involved is unknown and an allergic theory or histamine release cannot be substantiated.

DeOreo and others[57] reported their observations on 95 consecutive cases of molluscum contagiosum. In 10 of these cases a localized eczematous reaction was observed surrounding one or more of the molluscum contagiosum lesions. This reaction appeared one to eleven months after the appearance of the molluscum contagiosum, and the eczematous reaction subsided within one to three weeks after successful treatment of the original lesions. It is known that this disorder is caused by a virus and it is suggested that the reaction may be due to local sensitization to the elementary bodies or to soluble products of their metabolism.

Greenblatt[88] has discussed the occurrence of eczema at the onset of menstruation. He states that it may not respond to such preparations as progesterone, ammonium chloride or androgens plus supplemental therapy with reserpine or chlorpromazine. He recommends the intramuscular use of small doses of cortisonelike hormones such as Prednisone, 2.5 mg twice a day. This is administered orally throughout the cycle or during the last half of the cycle. In his experience, patients may respond to cyclic adrenocorticotropin given intramuscularly on the 20th, 23rd and 26th day of the cycle.

In Queries and Minor Notes[171] a case of eczema at the onset of the menstrual period in a 24-year-old woman was reported. The eruption

appears about two days before each menstrual period and persists for about two weeks. During pregnancy the patient was entirely free of the eruption. One theory of the etiology of premenstrual tension is that an insufficient amount of progesterone is secreted prior to menstruation. During pregnancy there is greatly increased progesterone production and this may be the reason for the absence of symptoms at this time. Progesterone should be tried for such patients, giving 10 mg every second day from days 14 through 24 of the menstrual cycle. Some patients have long-lasting relief after three or four months' treatment.

Greenhill and Freed (1941) believe that premenstrual distress is the result of sodium ion retention by the different tissues in the body under the influence of the ovarian steroids. Patients are advised to eliminate sodium and fluids during the last two weeks of the menstrual cycle and are given 0.6 gm of ammonium chloride three times daily.

Another method of treatment is the administration of methyltestosterone, 5 mg sublingually daily for ten days before the expected onset of menstrual flow (Freed, 1945). Removal of the ovaries was not recommended.

In response to a query[173] it was noted that nothing is known about the etiology of aphthous stomatitis or canker sores and there is no evidence to support the assumption that they are connected with any kind of nutritional deficiency. The origin of aphthous stomatitis has been thought to be allergic, psychosomatic, or infectious. Many workers suspect a virus, although it is clearly different from a herpes simplex virus. Distelheim and Sulzberger (1949) found that rinsing of the mouth with a solution of the broad-range antibiotics, Aureomycin or Terramycin, is exceedingly effective in combating this condition. Two soluble tablets of 50 mg each are dissolved per ounce of water, and the patient is instructed to use the solution as a mouth wash for several minutes. The solution should not be swallowed. Freshly prepared solution should be used and the procedure repeated every two to four hours until symptoms subside and healing is evident.

In a discussion of a patient with aphthosis, it was noted[53] that the use of a 5 per cent "dental" ointment of pyridoxine hydrochloride (Merck & Co.) resulted in symptomatic relief of oral and genital ulcers. This ointment does not prevent recurrences but often stops pain quickly and seems to shorten the course of the eruption.

Pillsbury and Pace[166] reported the case of a 36-year-old white man who had a 1 cm ulcer of the soft palate and tonsillar pillar. The ulcer had a yellow necrotic base. There were small irregular superficial ulcerations of the tip of the tongue with yellowish bases. Treatment, including Meticorten, had not produced a favorable response. In discussion it was suggested that trial diets should be employed. A patient with aphthous stomatitis was found to be allergic to peppermint and chocolate and another boy of 11 was found to be sensitive to corn and corn syrup. It was also noted that aphthous stomatitis is perhaps a better term than aphthous ulcer, since the term "aphthous" is the Greek word meaning ulcer.

Tuft and Ettelson[232] reported the case of a 37-year-old man with an allergic background who for many years had had frequent canker sores in the mouth. Extensive studies revealed that weak organic acids were the causative factor and a positive reaction to a crystal of citric acid was obtained on the mucous membrane of this patient's mouth, while controls were negative. Tests made with other organic acids showed

acetic acid to be strongly positive, tartaric acid mildly positive and lactic acid mildly positive. Tuft believes that this study is very important since it shows a proved reaction to a nonprotein substance which one would fail to get with a skin test. In this case mucous membrane reactions and avoidance of foods with acetic acid were followed by marked relief of canker sores. General "toxic" symptoms previously regarded as functional also disappeared when the weak organic acids were eliminated from the diet.

BIBLIOGRAPHY

1. Abramson, H. A.: Psychic factors in allergy and their treatment. Ann. Allergy, 14:145, 1956.
2. Abramson, H. A.: Psychogenic eczema in a child; report of a case. Ann. Allergy, 14:375-381 (July-Aug.) 1956.
3. Allington, H. V.: Eczematous and polymorphous hypersensitivity to light. Am. Pract. & Digest Treat., 7:1318, 1956.
4. Alt, W. J. and Spengler, J. R.: Severe systemic reactions to para-amino-salicylic acid: a case report and review of the literature. Ann. Int. Med., 45:541, 1956.
5. Arkins, J. A., Ruetz, P. P. and Squier, T. L.: Mephenesin (tolserol) sensitivity with demonstrable skin-sensitizing antibody in the serum. J. Allergy, 28:247, 1957.
6. Atkinson, W. B., Suskind, R. R. and Goldman, L.: Reaction of normal human skin to intradermally injected hydrocortisone; a histologic and histochemical study. A.M.A. Arch. Path., 62:8, 1956.
7. Austrian, C. R. and Boger, W. P.: Sensitization and subsequent desensitization to Probenecid (Benemid). A.M.A. Arch. Int. Med., 98:505, 1956.
8. Baer, R. L.: Current views on atopic dermatitis. New York J. Med., 56:1664, 1956.
9. Baer, R. L.: The present status of differentiation of allergic and nonallergic hypersensitivity to physical agents. Am. Pract. & Digest Treat., 7:1311, 1956.
10. Baer, R. L.: Correspondence. J. Allergy, 27:483, 1956.
11. Baer, R. L.: Letter to Editor. Ann. Allergy, 14:551, 1956.
12. Baird, K. A.: Allergy to bacterial products; a review of the literature. Ann. Allergy, 15:174, 1957.
13. Bauckus, H. H. and Gohringer, J. H.: Dermatitis of the hands. New York J. Med., 56:381, 1956.
14. Bernstein, I. L.: Anaphylaxis to heparin sodium: report of a case with immunologic studies. J.A.M.A., 161:1379, 1956.
15. Bierlein, K. J.: Repeated anaphylactic reactions in a patient highly sensitized to penicillin: a case report. Ann. Allergy, 14:35, 1956.
16. Bierly, M. Z., Jr.: Considerations of special interest to the allergist on the composition and production of poliomyelitis vaccine. Ann. Allergy, 14:349-359 (July-Aug.) 1956.
17. Blank, I. H.: Allergic hypersensitivity to an antiseptic soap. J.A.M.A., 160:1225, 1956
18. Blatt, H.: A review of the allergic response to microbes. Quart. Rev. Allergy, 10:496, 1956.
19. Blodgett, F. M., Burgin, L., Iezzoni, D., Gribetz, D., and Talbot, N. B.: Effects of prolonged cortisone therapy on the statural growth, skeletal maturation and metabolic status of children. New England J. Med., 254:636, 1956.
20. Bolam, R. M., and Burtt, E. T.: Flea infestation as a cause of papular urticaria; a preliminary investigation. Brit. M. J., 1:1130, 1956.
21. Bolton, F. G.: Thrombocytopenic purpura due to quinidine. II. Serologic mechanisms. Blood, 11:547, 1956.
22. Bolton, F. G., and Dameshek, W.: Thrombocytopenic purpura due to quinidine. I. Clinical studies. Blood, 11:527, 1956.
23. Brill, A.: Laryngeal edema and drugs. Correspondence. J.A.M.A., 160:1355, 1956.
24. Brown, E. A.: Progress in allergy: the reporting of drug toxicity. Part I. Ann. Allergy, 14:206, 1956.
25. Brunsting, H. A. and Eyster, W. H., Jr.: Allergic granulomatosis. Soc. Tr. A.M.A. Arch. Dermat. & Syph., 74:318, 1956.
26. Buffum, W. P.: Infantile eczema. Rhode Island M. J., 39:198, 1956.
27. Burke, J. O.: Personal communication.

28. Burrage, W. S., Greene, J. E., Burgin, L. B., Itkin, I. H., Novey, H. S., Engler, J. and Irwin, J. W.: Allergy, New England J. Med., 255:79, 1956.
29. Byrd, B.: Atopic eczema. A.M.A. Arch. Dermat. & Syph., 74:223, 1956.
30. Cahn, M. M. and Levy, E. J.: Ultraviolet light factor in chlorpromazine dermatitis. A.M.A. Arch. Dermat. & Syph., 75:38, 1957.
31. Calnan, C. D., and Wells, G. C.: Suspender dermatitis and nickel sensitivity. Brit. M. J., 1:1265, 1956.
32. Calnan, C. D. and Wilson, H. T.: Nylon stocking dermatitis. Brit. M. J., 1:147, 1956.
33. Campbell, E. W., Desy, L. and Dameshek, W.: A circulating anticoagulant as the primary manifestation of lupus erythematosus. Clin. Res. Proc., 5:231, 1957.
34. Canizares, O.: Contact dermatitis due to the acrylic materials used in artificial nails. A.M.A. Arch. Dermat. & Syph., 74:141, 1956.
35. Canizares, O. and Cipollaro, A. C.: Angioneurotic edema causing unilateral exophthalmos. Soc. Tr. A.M.A. Arch. Dermat. & Syph., 74:444, 1956.
36. Canizares, O. and Trilla, E.: Dermatitis venenata due to ragweed pollen. A.M.A. Arch. Dermat. & Syph., 75:905, 1957.
37. Caplin, I.: Chronic urticaria: the problem and its management. J. Indiana M.A., 49:1066, 1956.
38. Carmel, W. J., Jr. and Dannenberg, T.: Nonthrombocytopenic purpura due to Miltown (2-methyl-2-N-propyl-1,3 propanediol dicarbamate). New England J. Med., 255:770, 1956.
39. Chase, M.: The mechanism of sensitization. J. Allergy, 28:30, 1957.
40. Chase, M. W.: Discussion. Bull. New York Acad. Med., 32:240, 1956.
41. Chase, M. W., Slizys, I. S. and Allen, R. A.: The occurrence of multiple disseminated granulomata in sensitized animals. Presented at the 13th Annual Meeting of the American Academy of Allergy, Los Angeles, California, Feb. 4-6, 1957.
42. Chervinsky, P.: Erythema multiforme following poliomyelitis vaccination; report of a case. Ann. Allergy, 15:30, 1957.
43. Christianson, H. B. and Perry, H. O.: Reactions to chloral hydrate. A.M.A. Arch. Dermat. & Syph., 74:232, 1956.
44. Close, A. S. and Kory, R. C.: Cutaneous necrosis due to norepinephrine: mechanism and prevention. Clin. Res. Proc., 4:241, 1956.
45. Clyman, S. G.: Comparative effects of hydrocortisone and hydrocortisone-coal tar extract creams in cases of atopic dermatitis. Postgrad. Med., 21:309, 1957.
46. Cohen, A. S.: Acute Schönlein-Henoch purpura treated with prednisolone; report of a case. Brit. M. J., 1:143, 1957.
47. Cohen, S. G.: Trichophytin sensitivity of the immediate wheal type: report of a case with unusual manifestations and response to hydrocortisone. J. Allergy, 27:332, 1956.
48. Coleman, M., and Siegel, B. B.: Studies in penicillin hypersensitivity. III. The influence of parenterally administered antihistamines on contralateral passive transfer reactions to penicillin. J. Allergy, 27:27, 1956.
49. Comens, P.: Experimental hydralazine disease and its similarity to disseminated lupus erythematosus. J. Lab. & Clin. Med., 47:444, 1956.
50. Cormia, F. E., Worthington, E. and Sheard, C., Jr.: Granuloma of axilla (zirconium ?) from deodorant stick. A.M.A. Arch. Dermat. & Syph., 75:903, 1957.
51. Cornbleet, T., Barsky, S. and Del Busto, C.: Neurodermatitis treated with thorazine. Soc. Tr. A.M.A. Arch. Dermat. & Syph., 73:412, 1956.
52. Council on Pharmacy and Chemistry: Blood dyscrasias associated with chlorpromazine therapy. J.A.M.A., 169:287, 1956.
53. Curth, H. O.: Aphthosis: recurrent, oral and genital ulcerations; involvement of gastrointestinal tract. Soc. Tr. A.M.A. Arch. Dermat. & Syph., 73:401, 1956.
54. Davis, J. B., and Tachdjian, M.: Unique allergic response to sulfisoxazole (Gantrisin). Clinical Notes. J.A.M.A., 161: 228, 1956.
55. Dawson, C. R.: The chemistry of poison ivy. Tr. New York Acad. Sc., 18:427, 1956.
56. Delaunay, A., Hénon, M., Bazin, S. and Pelletier, M.: La properdine et son importance en immunologie; etat actuel de la question. Presse méd., 64:65, 1956.
57. DeOreo, G. A., Johnson, H. H., Jr. and Binkley, G. W.: An eczematous

reaction associated with molluscum contagiosum. A.M.A. Arch. Dermat. & Syph., 74:344, 1956.
58. Derbes, V. J. and Caro, M. R.: Localized eczema induced by house dust extract injections. A.M.A. Arch. Dermat. & Syph., 75:804, 1957.
59. Diamond, H. E.: Atopic dermatitis due to inhalants. New York J. Med., 57:754, 1957.
60. Editorial. Orally given antidiabetic sulfonamide compounds. J.A.M.A., 160: 1320, 1956.
61. Eisen, H. N.: Delayed allergic skin responses of the contact dermatitis type. Bull. New York Acad. Med., 32:239, 1956.
62. Epstein, E. and Claiborne, E. R.: Racial and environmental factors in susceptibility to Rhus. A.M.A. Arch. Dermat. & Syph., 75:197, 1957.
63. Epstein, S.: Contact dermatitis due to nickel and chromate: observations on dermal delayed (tuberculin-type) sensitivity. A.M.A. Arch. Dermat. & Syph., 73:236, 1956.
64. Epstein, S.: Contact dermatitis from neomycin. Correspondence. J.A.M.A., 160:1355, 1956.
65. Epstein, S.: Urticarial hypersensitivity to light. Am. Pract. & Digest Treat., 7:1326, 1956.
66. Epstein, S. and Pinkus, H.: Misleading patch tests; report of two cases. A.M.A. Arch. Dermat. & Syph., 75:260, 1957.
67. Epstein, W. L. and Kligman, A. M.: Pathogenesis of eosinophilic pneumonitis (Löeffler's syndrome). J.A.M.A., 162:95, 1956.
68. Favour, C. B.: Anti-inflammatory properties of a pyrimidine derivative, RO 2-5383/2. Clin. Res. Proc., 5:86, 1957.
69. Feinberg, A. R. and Feinberg, S. M.: Prednisone in allergic diseases. J.A.M.A., 160:264, 1956.
70. Feinberg, S. M. and Feinberg, A. R.: Allergy to penicillin. J.A.M.A., 160:778, 1956.
71. Fisher, A. A. and Shapiro, A.: Allergic eczematous contact dermatitis due to metallic nickel. J.A.M.A., 161:717, 1956.
72. Fisher, R. S.: The use of boric acid in dermatologic practice. A.M.A. Arch. Dermat. & Syph., 73:336, 1956.
73. Fitzgerald, J. D. and Irvine, A. H.: The use of cortisone and ACTH in serum sickness and penicillin reactions. . Canad. M.A.J., 74:46, 1956.
74. Foxworthy, D. T., Poske, R. M., Barton, E. M., Baker, L. A. and Montgomery, M. M.: Adrenocorticotropin and cortisone in the treatment of severe Reiter's syndrome. Ann. Int. Med., 44:52, 1956.
75. Freedman, A. L., Brody, E. A. and Barr, P. S.: Immunothrombocytopenic purpura due to quinidine: report of 4 new cases with special observations on patch testing. J. Lab. & Clin. Med., 48:205, 1956.
76. Frey, J. R. and Wenk, P.: Experimentelle Untersuchungen zur Pathogenese des Kontaktekzems. Dermatologica, 112:265, 1956.
77. Friedman, A. A.: Dermatitis of the breast from lead pencils. A.M.A. Arch. Dermat. & Syph., 73:384, 1956.
78. Friedman, H. T. and Marmelzat, W. L.: Adverse reactions to meprobamate. J.A.M.A., 162:628, 1956.
79. Gaillard, C. E.: The modern treatment of poison ivy. New York J. Med., 56:2255, 1956.
80. Garat, B. R., Landa, C. R., Richeri, O. F. R. and Tracchia, R. O.: Clinical, chemical, and pharmacologic relationships of antihistamines; a study of a new synthetic antihistaminic, carbinoxamine maleate (clistin maleate). J. Allergy, 27:57, 1956.
81. Gardner, L. I. and Tice, A. A.: Increased tissue histamine in urticaria pigmentosa: preliminary observations on the site of the biochemical error. Clin. Res. Proc., 4:158, 1956.
82. Gitlin, D., Hitzig, W. H. and Janeway, C. A.: Multiple serum protein deficiencies in congenital and acquired agammaglobulinemia. J. Clin. Invest., 35:1199, 1956.
83. Glaser, J.: Allergy in childhood. Springfield, Illinois, Charles C Thomas, 1956.
84. Godden, J. O., Clagett, O. T. and Andersen, H. A.: Sensitivity to alcohol as a symptom of Hodgkin's disease. J.A.M.A., 160:1274, 1956.
85. Goldman, L., Preston, R. H. and Muegel, H. R.: Dermatitis venenata from English ivy (Hedera helix). A.M.A. Arch. Dermat. & Syph., 74:311, 1956.
86. Grayson, L. D : The use of soap and detergents in skin diseases: an evaluation of a new soapless soap. Am. Pract. & Digest Treat., 7:269, 1956.
87. Green, T. W. and Early, J. Q.: Thrombocytopenic purpura resulting from sulfisoxazole (Gantrisin) therapy. J.A.M.A., 161:1563, 1956.

88. Greenblatt, R. B.: Eczema at onset of menstruation. J.A.M.A., 160:1186, 1956.
89. Griem, S. F. and Rothman, S.: Cutaneous sensitivity to cold. Am. Pract. & Digest Treat., 7:1335, 1956.
90. Grolnick, M.: Occupational contact dermatitis. New York J. Med., 56:1955, 1956.
91. Gropper, A. L.: Diphenylhydantoin sensitivity; report of a fatal case with hepatitis and exfoliative dermatitis. New England J. Med., 254:522, 1956.
92. Gumpel, R. C., Kristan, J. J. and Lipton, P.: The use of l-arterenol in a case of hypersensitivity to tetanus antitoxin. Ann. Int. Med., 44:406, 1956.
93. Healy, R. J. and McDonald, J. P.: Generalized allergy to protamine. New York J. Med., 56:720, 1956.
94. Herxheimer, A.: The nervous pathway mediating cholinogenic urticaria. Clin. Sc., 15:195, 1956.
95. Hill, L. W.: Atopic dermatitis. J. Allergy, 27:480, 1956.
96. Hinz, C. F., Jr. and Murphy, J. R.: Properdin levels in human disease. Clin. Res. Proc., 4:93, 1956.
97. Hirsch, P.: Adrenocortical steroids, their derivatives, and corticotropin, pharmacologic aspects, uses, and contraindications in dermatology. A.M.A. Arch. Dermat. & Syph., 73:342, 1956.
98. Hollander, L.: Vesicular dermatitis of the palms caused by colchicine. A.M.A. Arch. Dermat. & Syph., 75:872, 1957.
99. Holmes, C. R. and Stone, H. M.: Agranulocytosis due to chlorpromazine; report of a case with recovery. J. South Carolina M.A., 52:42, 1956.
100. Honey, M.: Systemic lupus erythematosus presenting with sulphonamide hypersensitivity reaction. Brit. M. J., 1:1272, 1956.
101. Høvding, G.: Yrkeseksem av klorpromazine. (Occupational eczema due to chlorpromazine). Tskr. Norske laegeforen., 76:250, 1956.
102. Humphrey, J. H. and Jaques, R.: The release of histamine and 5-hydroxytryptamine (serotonin) from platelets by antigen-antibody reactions (in vitro). J. Physiol., 128:9, 1955.
103. Hutner, L.: Oxytetracycline-hydrocortisone ointment (Terra-Cortril) in common dermatoses. Antibiotic Med. & Clin. Therapy, 3:326, 1956.
104. Irgang, S.: Nodular vasculitis; report of a case with clinical resemblance to papulonecrotic tuberculid. A.M.A. Arch. Dermat. & Syph., 74:673, 1956.
105. Isaacson, S., Gold, J. A. and Ginsberg, V.: Fatal aplastic anemia after therapy with nuvarone (3-methyl-5-phenylhydantoin). J.A.M.A., 160:1311, 1956.
106. Israel, H. L. and Sones, M.: The diagnosis of sarcoidosis with special reference to the Kveim reaction. Ann. Int. Med., 43:1269, 1955.
107. James, H. D., and Stanton, J. P.: Skin manifestations of drug allergy. Postgrad. Med., 21:485, 1957.
108. Jillson, O. F.: Hypersensitivity to heat. Am. Pract. & Digest Treat., 7:1332, 1956.
109. Jillson, O. F.: Allergic dermatitis produced by pathogenic and saprophytic fungi. Ann. Allergy, 15:14, 1957.
110. Johnston, T. G. and Cazort, A. G.: The practical management of contact dermatitis. South. M. J., 49:752, 1956.
111. Jordan, J. W. and Crissey, J. T.: Boric acid poisoning. A.M.A. Arch. Dermat. & Syph., 75:720, 1957.
112. Kalz, F. and Scott, A.: Hydrocortisone ointment bases; clinical evaluation of the effect of eleven vehicles containing one per cent hydrocortisone. A.M.A. Arch. Dermat. & Syph., 73:355, 1956.
113. Kennedy, C. B., Davis, F. H., Henington, V. M. and Sternberg, M. J.: Dermatitis medicamentosa due to antipyrine. A.M.A. Arch. Dermat. & Syph., 75:826, 1957.
114. Kerlan, I.: Foods, drugs, cosmetics and the allergist. J. Allergy, 27:391, 1956.
115. Kesten, B. M.: The effects of sunlight on the skin. J.A.M.A., 161:1565, 1956.
116. Klauder, J. V.: Some aspects of occupational dermatoses. J.A.M.A., 160:442, 1956.
117. Klauder, J. V. and Kimmich, J. M.: Sensitization dermatitis to carrots; report of cross sensitization phenomenon and remarks on phytophotodermatitis. A.M.A. Arch. Dermat. & Syph., 74:149, 1956.
118. Kligman, A. M.: Plastic band-aids for patch testing. A.M.A. Arch. Dermat. & Syph., 75:739, 1957.
119. Kraft, B., Howell, J. D. and Blumenthal, D.: A psychotherapist's integration into an allergic practice. Ann. Allergy, 15:168, 1957.
120. Krohn, S. E.: Anaphylactic shock from oral penicillin. New York J. Med., 56:1789, 1956.

121. Kurnick, N. B.: A rational therapy of systemic lupus erythematosus. Clin. Res. Proc., 4:54, 1956.
122. Kvorning, S. A. and Svandsen, I. B.: A synthetic detergent as a provocative agent in patch tests. J. Invest. Dermat., 26:421, 1956.
123. Lane, C. W. and Kost, L. B.: Sensitivity to artificial nails. A.M.A. Arch. Dermat. & Syph., 74:671, 1956.
124. Lapides, J. and Boyd, R. E.: The effect of intravenous benadryl in allaying allergic manifestations of 70 per cent urokon. J. Urol., 75:1016, 1956.
125. Larochelle, L. N. and Julien, J. M.: Quelques considérations sur la périarterite noueuse et sur son traitement par la conticotrophine. Laval méd., 21:164, 1956.
126. Lawrence, H. S.: The transfer in humans of skin sensitivity of the tuberculin type with components of disrupted leukocytes. Buil. New York Acad. Med., 32:236, 1956.
127. Leider, M.: Selected skin diseases of childhood. New York J. Med., 56:1961, 1956.
128. Leinassar, J. M.: Contact dermatitis due to chlorpromazine. Northwest. Med., 55:661, 1956.
129. Lentino, W., Zeitel, B. E., Jacobson, H. G. and Poppel, M. H.: Intravenously given urographic mediums. J.A.M.A., 161:606, 1956.
130. Levan, N. E. and Mundy, C. F.: Untoward reaction to meprobamate (Equanil). California Med., 85:190, 1956.
131. Levin, H. M. and Sutton, C. B.: A new steroid-antibiotic ointment: report of its use in 108 patients with dermatoses. Am. Pract. & Digest Treat., 7:594, 1956.
132. Lewe, I. A.: Granulomas of the axillae caused by deodorant. A.M.A. Arch. Dermat. & Syph., 75:765, 1957.
133. Lincoln, C. S., Jr.: Disseminated pathergic (allergic) granulomatosis; the histopathological picture of a cutaneous lesion: report of a case. A.M.A. Arch. Dermat. & Syph., 75:107, 1957.
134. Lipman, W. M.: The treatment of allergic diseases with the steroid hormones. Ann. Allergy, 14:365-374 (July-Aug.) 1956.
135. Lobitz, W. C., Jr. and Dobson, R. L.: Physical and physiological clues for diagnosing eczema. J.A.M.A., 161:1226, 1956.
136. Lobitz, W. C., Jr., Heller, M. L. and Dobson, R. L.: Physiologic studies in atopic dermatitis; disseminated neurodermatitis. II. The effect of denervation on the "delayed blanch phenomenon." A.M.A. Arch. Dermat. & Syph., 75:228, 1957.
137. Lorincz, A. L.: Hypersensitivity to trauma. Am. Pract. & Digest Treat., 7:1314, 1956.
138. Loveless, M. H., and Fackler, W. R.: Wasp venom allergy and immunity. Ann. Allergy, 14:347-366 (Sept.-Oct.) 1956.
139. Loveman, A. B. and Fliegelman, M. T.: Dermatitis medicamentosa; reaction from hydrocortisone's suspension vehicle (sodium carboxymethyl cellulose). A.M.A. Arch. Dermat. & Syph., 74:426, 1956.
140. Magnus, I. A. and Thompson, R. H.: Cholinesterase levels in the skin in cholinogenic urticaria and pruritus. Brit. J. Dermat., 68:283, 1956.
141. Marchionini, A. and Borelli, S.: Klimabehandlung der Neurodermatis disseminata. Deut. med. Wchnschr., 81:811, 1956.
142. Markow, H.: The cytology of respiratory secretions in the management of allergy. New York J. Med., 56:1454, 1957.
143. Marmor, J., Ashley, M., Tabachnick, N., Storkan, M. and McDonald, F.: The mother-child relationship in the genesis of neurodermatitis. A.M.A. Arch. Dermat. & Syph., 74:599, 1956.
144. Martin, W. J., Heilman, F. R., Nichols, D. R., Wellman, W. E. and Geraci, J. E.: Novobiocin (streptonivicin, cathomycin): further observations. Proc. Staff Meet. Mayo Clin., 31:416, 1956.
145. Mathews, K. P., Hemphill, F. M., Lovell, R. G., Forsythe, W. E. and Sheldon, J. M.: A controlled study on the use of parenteral and oral antihistamines in preventing penicillin reactions. J. Allergy, 27:1, 1956.
146. Mauer, A. M., DeVaux, W. and Lahey, M. E.: Neonatal and maternal thrombocytopenic purpura due to quinine. Pediatrics, 19:84, 1957.
147. Mazzitello, W. F. and Good, R. A.: Editorial: Agammaglobulinemia. Minnesota Med., 39:308, 1956.
148. McCombs, R. P., Patterson, J. F. and MacMahon, H. E.: Syndromes associated with allergic vasculitis. New England J. Med., 255:251, 1956.
149. Mello, J. F., de and Mendes, E.: Reação do tipo anafilatico após uma prova intradérmica com penicilina. Rev. Ass. med. brasil., 2:145, 1956.

150. Mitchell, J. H., Smith, D. L. and Mayers, R. A.: Is chronic urticaria an allergic disorder? Ann. Allergy, 15:128, 1957.
151. Morginson, W. J., Rich, C. O., Eskelson, Y. D., Kirkman, L. W., Utterback, M., Burton, A. M. and Coletti, J. M.: Dyclonine hydrochloride: a new topical antipruritic agent. Postgrad. Med., 19:605, 1956.
152. Morris, G. E.: Urticaria following exposure to ammonia fumes. A.M.A. Arch. Indust. Health, 13:480, 1956.
153. Morris-Owen, R. M.: Treatment of contact dermatitis due to handling antibiotics. Brit. M. J., 1:654, 1956.
154. Mullins, J. F., Cohen, I. M., and Farrington, E. S.: Cutaneous sensitivity reactions to chlorpromazine. J.A.M.A., 162:946, 1956.
155. Nasou, J. P. and Romansky, M. J.: Side effects of antibiotic therapy. Postgrad. Med., 19:341, 1956.
156. Noojin, R. O.: The dermatologic management of pruritus. South. M. J., 49:149, 1956.
157. Olansky, S., Smith, J. G., Jr. and Hansen-Pruss, O. C. E.: Fatal vaccinia associated with cortisone therapy. J.A.M.A., 162:887, 1956.
158. Origin of antibiotics. Lancet, 1:89, 1956.
159. Osborn, R. A. and Tusing, T. W.: Multiple patch in place of individual patch in skin testing. A.M.A. Arch. Dermat. & Syph., 74:667, 1956.
160. Pardo-Castello, V.: Dermatology in a tropical rural zone; reference to occupational dermatoses. A.M.A. Arch. Dermat. & Syph., 74:115, 1956.
161. Passenger, R. E., Spain, W. C. and Strauss, M. B.: Aqua ivy; toxicity studies on the guinea pig and treatment of sensitive cases. J. Allergy, 27:409, 1956.
162. Pastor, B. H. and Tetreault, A. F.: Agranulocytosis and scarlatiniform eruption due to phenindione. J.A.M.A., 161:873, 1956.
163. Peacock, L. B. and Davison, H. M.: Observations on iodide sensitivity. Ann. Allergy, 15:158, 1957.
164. Peck, S. M. and Palitz, L. L.: Sensitization to facial tissues with urea-formaldehyde resin (wet-strength). J.A.M.A., 160:1226, 1956.
165. Peters, G. A., Henderson, L. L. and Prickman, L. E.: Anaphylactic reactions to penicillin: case report with certain immunologic observations. Ann. Allergy, 15:135, 1957.
166. Pillsbury, D. M. and Pace, K. B.: Recurrent severe aphthous stomatitis. A.M.A. Arch. Dermat. & Syph., 75:310, 1957.
167. Pinkus, H. and Botvinick, I.: Deodorant stick eruption (zirconium granuloma) of axillae. A.M.A. Arch. Dermat. & Syph., 75:756, 1957.
168. Popoff, N. and Wheelock, M. C.: Relapsing febrile nodular nonsuppurative panniculitis: Pfeifer-Weber-Christian disease; report of three cases. A.M.A. Arch. Int. Med., 97:39, 1956.
169. Preston, R. H. and Flatt, R.: Intravenous hydrocortisone hemisuccinate and prednisolone hemisuccinate. A.M.A. Arch. Dermat. & Syph., 74:613, 1956.
170. Prickman, L. E. and Lofgren, K. A.: An emergency set to combat anaphylaxis. J.A.M.A., 161:1159, 1956.
171. Queries and Minor Notes: Eczema at onset of menstruation. J.A.M.A., 160:341, 1956.
172. Ibid. Tuberculin reaction. J.A.M.A., 160:920, 1956.
173. Ibid. Canker sores. J.A.M.A., 161:300, 1956.
174. Ibid. Prophylaxis of ivy poisoning. J.A.M.A., 161:768, 1956.
175. Ibid. Sensitivity to rubber gloves. J.A.M.A., 161:931, 1956.
176. Ibid. Poison ivy prophylaxis. J.A.M.A., 161:1212, 1956.
177. Ibid. Allergy to penicillin. J.A.M.A., 161:1343, 1956.
178. Ibid. Allergy to sunlight. J.A.M.A., 161:1517, 1956.
179. Ibid. Anaphylactic reaction after injection of vitamin K. J.A.M.A., 163:410, 1957.
180. Rajka, E.: Zur Pathogenese des urtikariell-entzündlichen Juckens. IV. Beiträge zur Theorie des zweiphasigen Juckmechanismus; vergleichende Untersuchungen mit anderen Hautaxonreflexen. Dermatologica, Basel, 112:189, 1956.
181. Random Notes. Reactions to meprobamate. Rev. Allergy, 11:2, 1957.
182. Rapaport, J.: "Urticaria" due to cold. Soc. Tr. A.M.A. Arch. Dermat. & Syph., 75:607, 1957.
183. Rappaport, B. Z.: Studies on atopic dermatitis. II. Melanin distribution and dopa oxidase reaction. A.M.A. Arch. Path., 61:318, 1956.
184. Ratner, B.: Allergic factors in infantile eczema. New York J. Med., 56:1501, 1956.
185. Ratner, B., Crawford, L. W. and Flynn, J. G.: Allergy in the infant and preschool child. A.M.A. Am. J. Dis. Child., 91:593, 1956.

186. Rein, C. R. and Bodian, E. L.: A clinical evaluation of prednisone in the treatment of dermatoses. A.M.A. Arch. Dermat. & Syph., 73:378, 1956.
187. Reisner, E. H., Jr. and Morgan, M. C.: Thrombocytopenia following acetazolamide (Diamox) therapy. J.A.M.A., 160:206, 1956.
188. Reyer, W. A.: Periorbital dermatitis following adhesive tape strapping of the lower extremities. Ann. Allergy, 15:144, 1957.
189. Ridolfo, A. S. and Kirtley, W. R.: Clinical experiences with carbutamide, an orally given hypoglycemic agent; preliminary report. J.A.M.A., 160:1285, 1956.
190. Robinson, H. M., Jr., Robinson, R. C. V. and Strahan, J. F.: Hydroxyzine (Atarax) hydrochloride in dermatological therapy. J.A.M.A., 161:604, 1956.
191. Rodnan, G. P., Black, R. L., Bollet, A. J. and Bunim, J. J.: Observations on the use of prednisone in patients with progressive systemic sclerosis (diffuse scleroderma). Ann. Int. Med., 44:16, 1956.
192. Rogachefsky, H., Rosenthal, S. A., Litt, J. Z. and Baer, R. L.: Trichophytin reaction after exposure to dermatophytes. A.M.A. Arch. Dermat. & Syph., 74:606, 1956.
193. Rostenberg, A., Jr.: Primary irritant and allergic eczematous reactions. A.M.A. Arch. Dermat. & Syph., 75:547, 1957.
194. Rostenberg, A., Jr.: Solar urticaria. Soc. Tr. A.M.A. Arch. Dermat. & Syph., 75:773, 1957.
195. Rostenberg, A., Jr. and Iverson, V.: Cutaneous allergic vasculitis. Soc. Tr. A.M.A. Arch. Dermat. & Syph., 75:287, 1957.
196. Rostenberg, A., Jr., McCraney, H. C. and Bluefarb, S. M.: Immunologic studies in the lymphoblastomas. II. The ability to develop an eczematous sensitization to a simple chemical and the ability to accept passive transfer antibody. J. Invest. Dermat., 26:209, 1956.
197. Rubin, L., Slepyan, A. H., Weber, L. F. and Neuhauser, I.: Granulomas of the axillae caused by deodorants. J.A.M.A., 162:953, 1956.
198. Salomon, A., Appel, B., Collins, S. F., Herschfus, J. A. and Segal, M. S.: Sarcoidosis: pulmonary and skin studies before and after ACTH and cortisone therapy. Dis. Chest, 29:277, 1956.
199. Sams, W. M.: Contact photodermatitis.: A.M.A. Arch. Dermat. & Syph., 73:142, 1956.
200. Sandberg, A. A., Moore, G. E., Bender, M., and Tarail, R.: The intravenous administration of large doses of immune globulin to human subjects. Clin. Res. Proc., 4:92, 1956.
201. Sanger, M.D., and Ehrlich, D. E.: A method of reducing reactions in intravenous pyelography with an antihistamine. Ann. Allergy, 14:254, 1956.
202. Schick, G., and Virks, J.: Agranulocytosis associated with chlorpromazine therapy: report of a case and review of the literature. New England J. Med., 255:798, 1956.
203. Schiller, I. W., and Lowell, F. C.: Toxicologic and clinical appraisal of Buclizine, a new antihistaminic compound. J. Allergy, 27:63, 1956.
204. Schwartz, I. H.: Brief recording: Observations on urticaria in childhood. New England J. Med., 255:771, 1956.
205. Schwartz, L.: Allergic occupational dermatitis. Quart. Rev. Allergy, 10: 238, 1956.
206. Scott, A., and Kalz., F.: The penetration and distribution of C 14-hydrocortisone in human skin after its topical application. J. Invest. Dermat., 26:149, 1956.
207. Seville, R. H.: Chlorpromazine dermatitis in nurses. Brit. J. Dermat., 68: 332, 1956.
208. Shands, W. C., and Johnston ,J. H., Jr.: Anaphylactic shock from intrapleural streptokinase-streptodornase. J. Thoracic Surg., 31:320, 1956.
209. Shane, A. M., and Hirsch, S.: Three cases of meprobamate poisoning. Canad. M. A. J., 74:908, 1956.
210. Shanon, J., and Sagher, F.: Sabra dermatitis; an occupational dermatitis due to prickly pear handling simulating scabies. A.M.A. Arch. Dermat. & Syph., 74:269,1956.
211. Sherman, W. B.: Allergy to drugs. New York J. Med., 56:3527, 1956.
212. Siegel, B. B., and Coleman, M.: Studies in penicillin hypersensitivity. IV. Antigenic properties of altered procaine penicillin. J. Allergy, 28:264, 1957.
213. Siegel, S. C., Birnberg, V., and Kelley, V. C.: Prednisone in the treatment of allergic disorders in children. A.M.A. Am. J. Dis. Child., 91:454, 1956.
214. Singleton, A. O., Jr., and Little, H. M., Jr.: The use of an antihistamine agent in preventing serum reactions following the injection of tetanus antitoxin. Surgery, 40:784, 1956.

215. Smith, C. C.: Prednisolone ointment and hydrocortisone ointment; comparative effectiveness in dermatological therapy. A.M.A. Arch .Dermat. & Syph., 74:414, 1956.
216. Smith, J. M., and Skaggs, J. T.: C-reactive protein in allergic diseases. J. Allergy, 27:338, 1956.
217. Smith, S. F.: Clinical appraisal of new antihistamine in allergic disease. Ann. Allergy, 15:25, 1957.
218. Spanoudis, S., Eichbaum, F., and Rosenfeld, G.: Inhibition of the local Shwartzman reaction by dicumarol. J. Immunology, 75:167, 1955.
219. Spring, M.: Skin eruptions following the use of Diamox. Ann. Allergy, 14:41, 1956.
220. Steinberg, C. L., and Roodenburg, A. I.: Metacortandracin (meticorten) in the treatment of disseminated lupus erythematosus and periarteritis nodosa. Ann. Int. Med., 44:316, 1956.
221. Steinkamp, R., Moore, C. V., and Doubek, W. G.: Thrombocytopenic purpura caused by hypersensitivity to quinine. J. Lab. & Clin. Med., 45:18, 1955.
222. Stewart, B. L., and Rowe, H. J.: Nitrofurantoin (Furadantin) in treatment of urinary tract infections. J.A.M.A., 160:1221, 1956.
223. Strauss, J. S., and Kligman, A. M.: The relationship of atopic allergy and dermatitis. A.M.A. Arch. Dermat. & Syph., 75:806, 1957.
224. Stritzler, C., and Samuels, L.: Urticaria caused by sensitivity to saccharin. Soc. Tr. A.M.A. Arch. Dermat. & Syph., 74:433, 1956.
225. Stubenrauch, G. O., Dalton, J. E., Armstrong, B., and Starcs, H.: Clinical evaluation of the therapeutic effects of a combined antibiotic ointment in pyodermas. J. Indiana M. A., 49:1063, 1956.
226. Sulzberger, M. B.: On the adrenal cortical steroids in relation to allergic dermatoses. New York J. Med., 56:1827, 1956.
227. Swanson, F.: Clinical evaluation of a new neutral detergent bar. J.A.M.A., 162:459, 1956.
228. Symon, W. E., Rohn, R. J., and Bond, W. H.: Some observations on hyperglobulinemic purpura (Waldenstrom's syndrome). Clin. Res. Proc., 5:158, 1957.
229. Tetreault, A. F., and Beck, I. A.: Anaphylactic shock following intramuscular thiamine chloride. Ann. Int. Med., 45:134, 1956.
230. Theodore, F. H.: Eczema of the eyelids. Ann. Allergy, 14:484, 1956.
231. Theriault, J. C.: A fatality associated with chlorpromazine (Largactil) therapy. Canad. M. A. J., 74:148, 1956.
232. Tuft, L., and Ettelson, L. N.: Canker sores from allergy to weak organic acids (citric and acetic). J. Allergy, 27:536, 1956.
233. Tuft, L., and Santor, G. F.: Stomatitis from allergy to acrylic denture: report of a case. J. Allergy, 27:261, 1956.
234. Underwood, L. C.: Fatal bone marrow depression after treatment with acetazolamide (Diamox). J.A.M.A., 161:1477, 1956.
235. Vollmer, H.: Topical use of fludrocortisone acetate in allergic dermatitis. A.M.A. Arch. Dermat. & Syph., 74:300, 1956.
236. Von Haam, E., and Mallette, F. S.: Skin testing of industrial compounds; development of polyvalent sensitivity. Am. Indust. Hyg. A. Quart., 16:324, 1955.
237. Waalkes, T. P., Weissbach, H., Bozicevich, J., and Udenfriend, S.: The release of serotonin and histamine during anaphylaxis in the rabbit. Clin. Res. Proc., 5:137, 1957.
238. Walsh, J. J., Linn, R. H., and Derbes, V. J.: Pyrexia due to isonicotinic acid hydrazide. J. Allergy, 27:548, 1956.
239. Wartzki, I. M., and Entwisle, B. R.: Topical hydrocortisone therapy in diseases of the skin: a clinical evaluation. Med. J. Australia, 1:318, 1956.
240. Weidman, A. I., and Sawicky, H. H.: Nummular eczema. A.M.A. Arch. Dermat & Syph., 73:58, 1956.
241. Weiner, R. G., Necheles, J. R., and Stanka, H.: Anaphylaxis following oral administration of penicillin. Am. Pract. & Digest Treat., 7:377, 1956.
242. Weinstock, I., and Albin, M. B.: Auto observation of a near fatal penicillin reaction in a physician. New York J. Med., 56:1825, 1956.
243. Weiss, W.: The nicotinic acid skin reaction in acute inflammatory disease. Clin. Res. Proc., 4:22, 1956.
244. Welch, H., Lewis, C. N., Putnam, L. E., and Randall, W. A.: A study of the sensitizing potential of novobiocin. Antibiotic Med., 3:27, 1956.
245. Winter, C. C., and Taplin, G. V.: Prevention of acute allergic and febrile

reactions to blood transfusions by prophylactic use of an antihistamine plus an antipyretic. Ann. Allergy, 14:76, 1956.
246. Wintrobe, M. M., and Cartwright, G. E.: Blood disorders caused by drug sensitivity. A.M.A. Arch. Int. Med., 98:559, 1956.
247. Wirtschafter, Z. T., Gaulden, E. C., and Williams, D W.: Cold allergy associated with cryoproteinemia. A.M.A. Arch. Dermat. & Syph., 74:302, 1956.
248. Wise, R. E., and O'Brien, R. G.: Interpretation of the intravenous cholangiogram. J.A.M.A., 160:819, 1956.
249. Wiseman, R. D., and Adler, D. K.: Acetic acid sensitivity as a cause of cold urticaria. J. Allergy, 27:50, 1956.
250. Withers, O. R., and Hale, R..: Progress in allergy: food allergy; a review of the literature. Ann. Allergy, 14:384-456 (Sept.-Oct.) 1956.
251. Wittich, F. W.: Diphemanil methylsulfate cream plain and with hydrocortisone in the treatment of various skin diseases. Ann. Allergy, 14:69, 1956.
252. Wolf, J.: Cryoglobulinemia. Soc. Tr. A.M.A. Arch. Dermat. & Syph., 73: 639, 1956
253. Wysham, D. N., Mulhern, M. E., Navarre, G. C., LaVeck, G. D., Kennan, A. L., and Giedt, W. R.: Epidemiologic studies of pyoderma neonatorum. Clin. Res. Proc., 5:201, 1957.
254. Youngblood, V. H., Williams, J. O., and Tuggle, A.: Reactions due to intravenous urokon. J. Urol., 75:1011, 1956.

WATCH FOR THESE ARTICLES IN FUTURE ISSUES

Clinical Evaluation of a New Long-Acting Preparation in Allergic Disorders. By Jerome Miller, M.D.

Is Serous Otitis Media Due to Allergy or Infection? By Irwin A. Solow, M.D.

Para-bromdylamine Maleate (Dimetane®). A Clinical Evaluation. By J. Warrick Thomas, M.D.

Allergy and Submarine Medicine, with Reference to Aerotitis Media. By Norman W. Clein, M.D.

Smoking and Chronic Respiratory Disorders. Results of Abstinence. By Oscar Swineford, Jr., M.D.

Histamine Cephalalgia and Its Relation to Migraine. By Leon Unger, M.D.

Allergy as a Cause of Genitourinary Symptoms. Clinical Considerations. By Clyde K. Walter, M.D.

Studies on Urticaria of Serum-Sickness Type, Using Penicillin Combined with Gamma Globulin as Allergen. By George Rajka, Jr., M.D., and Elisabeth Vincze, M.D.

Editorial

The opinions expressed by the writers of editorials in the ANNALS *do not necessarily represent the group opinion of the Board or of the College.*

STANDARD HUMAN BEINGS VS STANDARD MEASUREMENTS

In a recent issue of *Science* (126:453, September 1957), R. J. Williams discusses a fact which has "received little or no attention in the application of statistical methods to the study of human beings."

We use ten measurements (and the 50 per cent medial range), then only one subject in 1,024 is "standard." When the same ten measurements and a medial 95 per cent are chosen, then six out of ten subjects are standard.

"There are many areas," he writes, "where the aforementioned ideas are applicable and where the concept of standard individuals is inherent whether or not it is overtly expressed."

Dr. Williams points out, for example, that the twelve items of the "Recommended daily allowances" and the "Minimum daily requirements" set up by the Food and Nutrition Board of the U. S. Food and Drug Administration would be satisfactory on this basis for only 28 per cent of the population. When the number of items (or measurements) increases, the discrepancy between the validity of the items and "their validity as a group increases."

He ends by asking, "Does not a substantial amount of our scientific thinking involve this questionable concept?"

Doesn't it?

EXPERIMENTAL EXACERBATION OF ATOPIC DERMATITIS

How many allergists have been puzzled by the fact that patients with typical atopic eczema so often fail to respond to elimination diets and specific hyposensitization procedures, and yet demonstrate exacerbations from ingestion or inhalation of what are known to be specific allergens? When the patient's skin is clear, the same allergens are ingested or inhaled often without effect. In an ingenious experiment, Strauss and Kligman† give us a partial answer to this question.

As subjects, they used eight adult men free of eczema but demonstrating strong skin-test reactions, by standard scratch tests, to either short ragweed or crab extract. Seven of the patients were defined as atopic because of previous hay fever or bronchial asthma.

When crab or ragweed extracts were applied topically every day for three weeks, they failed to produce a dermatitis although percutaneous

†Strauss, John S., and Kligman, Albert M.: Atopic dermatitis. New England J. Med., 256:1002 (May 27) 1957.

absorption was proved by the occurrence of urticaria, hay-fever symptoms and bronchial asthma.

Rhus toxicodendrom antigen was then applied to the skins of the same subjects, who happened to be sensitive to poison ivy, to which they responded with typical, sharp patches of allergic contact dermatitis.

The atopens, that is the crab and short ragweed extracts, were then applied as follows:

"Daily topical application of 1:10 unadulterated whole-protein extract of crab and 1:20 pollen extract of short ragweed; intranasal instillation of the same concentrations of atopens twice daily; and subcutaneous injections of the same agents in gradually increasing doses three times a week. In six of the eight subjects, exposure by one or more of these routes produced a definite exacerbation of the dermatitis accompanied by marked itching and often a prolongation of the healing time. Particularly noteworthy in two subjects was the transformation, due to scratching, of the patch of dermatitis into a typical lichenified neurodermatitis.

They quote, as part explanation, the work of Menkin* who showed that blood-borne foreign proteins were "selectively concentrated and fixed in areas of inflammation."

"Normally," the authors say, in the subjects studied, "the reaction would be a wheal, but this is masked by the dermatitis. All that happens is an intensification of the primary dermatitic process."

They contend against the "deeply entrenched notion that the dermatitis is the *result* of the atopy." Rather they feel that "atopy is frequently associated with a characteristic type of dermatitis but is not its basic cause." The occasional patient benefited by hyposensitization may be attributed to removal of the secondary factors.

If, in their patients, the area of contact dermatitis after exposure to the positive skin test, two allergens and scratching was changed into an area of typical neurodermatitis, we must look on our atopically eczematous patients with new eyes. The removal or elimination of secondary factors which has always been considered important becomes more so since they may actually be primary reasons for the disorders.

The inability experimentally to induce the atopic type of eczematous dermatitis in man or animal which has so long delayed research in this field need no longer be a barrier to new studies to the benefit of these long-suffering patients.

*Menkin, V. J.: Exper. Med., 52:201-203, 1930.

Papers of Interest

Wintrobe, M. M., and Cartwright, G. E.: Blood disorders caused by drug sensitivity. Arch. Int. Med., 98:559-566, 1956.

A list of the drugs and a description of the mechanisms by means of which they may cause blood disorders is given.

Riley, J. F., and West, G. B.: Skin histamine: its location in the tissue mast cells. Arch. Dermat. & Syph., 74:471, 1956.

The bulk of the extractable histamine in the skin of man is located in the tissue mast cells.

Preston, R. H., and Flatt, R.: Intravenous hydrocortisone hemisuccinate and prednisolone hemisuccinate: their use in acute severe dermatological conditions. Arch. Dermat. & Syph., 74:613, 1956.

Intravenous hydrocortisone hemisuccinate and prednisolone hemisuccinate are valuable for initial corticosteroid therapy of acute severe dermatologic conditions.

Epstein, S.: Contact dermatitis from neomycin due to dermal delayed (tuberculin-type) sensitivity. Dermatologica, 113:191-201, 1956.

Ten cases of contact dermatitis apparently were due to dermal delayed (tuberculin-type) and not to epidermal sensitivity. Dermatitis of this type often appears as an aggravation of the pre-existing condition rather than an easily recognized acute secondary contact dermatitis.

Brooks, G. W.: Experience with the use of chlorpromazine and reserpine in psychiatry. New England J. Med., 254:1119 (June 14) 1956.

During the treatment of 386 psychotic women for sixteen months, toxic reactions were noted in 18 per cent of those taking reserpine, 30 per cent of those treated with chlorpromazine, and 56 per cent of those taking both. Toxic effects were relieved with trihexyphenidyl, 5 to 15 mg daily, or methyl-phenidylacetate, 30 to 120 mg daily, or a combination of both.

Bräutigam, W.: Über die psychosomatische Spezifität des Asthma bronchiale. Psyche, 8:9, 1954-55 (In German).

The author believes that no illness exists *per se*, but only occurs as an answer to an inner or outer call for action. He records 220 hours of psychoanalytic treatment of a patient with asthma, hay fever, and eczema. The treatment resulted in a change of personality and freedom from symptoms. It is his belief that, physiologically and psychologically, the allergic patient shuts himself against the foreign, dangerous and hostile world. He is not convincing.

Feinberg, R. J.; Davison, J. D.; and Flick, J. A.: The detection of antibodies in hay fever sera by means of hemagglutination. J. Immunol., 77:279 (Oct.) 1956.

Antibodies in the sera of hay fever patients against pollen antigens can be measured, *in vitro*, by adsorbing the antigen onto tanned erythrocytes and using such antigen-coated cells in a hemagglutination test. Such antibodies occur chiefly in patients who have received specific hyposensitization, but may be present in untreated subjects. The hemagglutinating antibody is not identical with reagin.

Schick, G., and Virks, J.: Agranulocytosis associated with chlorpromazine therapy. New England J. Med., 255:798-802 (Oct. 25) 1956.

A review of the twenty-one cases reported in the literature, of whom eight died. The occurrence of jaundice and agranulocytosis when concomitant is highly fatal.

Stroud, G. M.: Drug eruptions due to meprobamate. New England J. Med., 256:354-355 (Feb. 21) 1957.

Describes five cases of drug eruptions, of which three were diffuse, morbilliform erythemas and two were erythema multiforme. In one patient, there was fever and syncope. Response to hydrocortisone intravenously and prednisolone by mouth was rapid.

Høvding, G.: Occupational eczema from chlorpromazine. Tidsskr. norske laegefor., 76:250-251 (Apr. 15) 1956 (In Norwegian).

Lists seven methods of reducing contact dermatitis of nursing staff.

Wartzki, I. M., and Entwisle, B. R.: Topical hydrocortisone therapy in diseases of the skin: a clinical evaluation. M. J. Australia, 1:318-326 (Feb. 26) 1956.

One hundred patients were treated with topical hydrocortisone. The best results were obtained in the treatment of labial erythema multiforme, papular urticaria, eczema of the face and the scrotum, pruritus ani and vulvae, and intertrigo of the genitocrural and gluteal folds. Response was poor in Besnier's prurigo, discoid eczema, and otitis externa. Two patients with scrotal eczema and two with pruritus ani and intertrigo of the genitocrural and gluteal folds responded with exacerbations.

PAPERS OF INTEREST

May, J. R., and Oswald, N. C.: Long-term chemotherapy in chronic bronchitis. Lancet, II:814, 1956.

Twenty-two of thirty-seven cases of advanced purulent bronchitis responded "strikingly" to continuous tetracycline or oxytetracycline treatment. Side effects sufficiently severe to necessitate cessation of treatment occurred in two patients.

Rinsley, D. B.: Vasomotor lability as studied in patients with disseminated neurodermatitis. Internat. Rec. Med., 170:27-32, 1957.

The basal (resting) blood pressure and the blood pressure after thirty and sixty seconds of immersion of the hand in ice water, and the time required for the blood pressure to return to the basal value were all measured in twelve patients with disseminated neurodermatitis and twenty controls. All physical findings were the same excepting that the patients with disseminated neurodermatitis required a longer time to return to basal sphygmic levels. It is suggested that this vasomotor lability has a possible relationship to anxiety, frustration and, as well, to dermatologic disorders, all of which should be explored.

Fried, B. M.: The structure of the respiratory (terminal) portion of the lungs. Arch. Int. Med., 98:691-699, 1956.

The respiratory epithelial cells lining the walls of the air sacs constitute the defensive mechanisms of the lungs, assuming the functions of the ameboid phagocytic cells participating in the formation of the granuloma of tuberculosis. Their other functions are listed.

Surber, J. R.: Chronic bacterial allergy of the perinasal sinuses: a report of sixty-five cases. Arch. Otolaryng., 64:351-360.

There have been three groups of allergic responses described by the author, namely: anaphylactic, eczematous and bacterial. Chronic sinus disease belongs in the third. He suggests medical treatment except when surgery is absolutely necessary. Patients do best with both immunization and desensitization.

Phillips, A. M.; Phillips, R. W.; and Thompson, J. L.: Chronic cough: Analysis of etiologic factors in a survey of 1,274 men. Ann. Int. Med., 45:216-231 (Aug.) 1956.

Study of environmental factors, previous pulmonary infections, smoking habits and age of two groups indicates re-evaluation needed to determine the importance of each in cause of chronic cough.

Cohen, I. M., and Nash, J. B.: Photosensitization by chlorpromazine. Psychiat. Res. Rep., 1:11-13 (July) 1955.

A significant percentage of patients receiving chlorpromazine by oral or parenteral routes exhibited more intense erythematous reaction to ultraviolet radiation than did untreated patients.

Siegel, S. C.; Birnberg, V.; and Kelley, V. C.: Prednisone in the treatment of allergic disorders in children. J. Dis. Child., 91:454-459 (May) 1956.

A study of sixteen allergic children under eleven years treated with prednisone proved effective in temporary symptomatic relief of asthma and atopic eczema. Possible side effects require certain precautions.

Pace, W. G.: The evaluation of a new nasal decongestant. Mil. Med., 118:34-36 (Jan.) 1956.

Side effects were minimal in study of a new nasal decongestant, tetrahydrozoline hydrochloride, used in 0.1 per cent solution, in nasal congestion of sixty officers and enlisted men. No cases of rebound congestion of the nasal mucosa were noted.

Heller, Paul; Kellow, William F.; and Chomet, Bernhard; Needle biopsy of the parietal pleura. New England J. Med., 255:684 (Oct.) 1956.

Needle biopsy of the parietal pleura appears to be a useful technic in the differential diagnosis of pleural effusion, helpful in the confirmation of the report of the first twenty patients who were subjected to this procedure. The histologic diagnosis was caseating granuloma in five patients, malignant neoplasm in four, and nonspecific fibrosis in nine.

Levine, E. R.: A more direct liquefaction of bronchial secretion by aerosol therapy. Dis. of Chest, 31:155-168 (Feb.) 1957.

After careful investigation of four classes of aerosols a solution was prepared which contains 0.125 per cent of the detergent Tergitol 08 (sodium 2-hexylethylsulfate) and 0.1 per cent of potassium iodide in sterile water. The results on ninety-six patients are reported.

Ordman, D.: The climate factor in perennial respiratory allergy and its relation to house dust sensitivity. Internat. Arch. Allergy, 9:129-145 (No. 3-4) 1956.

The author raises the question as to whether patients with "climatic" respiratory allergy are not affected by a combination of temperature and humidity which may render potential sensitizing substances such as house dust more highly allergenic.

News Items

POSTGRADUATE COURSE IN ALLERGY

A series of conferences, sponsored by the University of Nebraska College of Medicine, will be given in Omaha on May 8 and 9, 1958. The registration fee is twenty dollars.

Pediatric Allergy will be the subject of the first morning's speakers. Adult Allergy will be discussed during the second morning. The two afternoons will be devoted to miscellaneous aspects of allergy. The faculty includes seven members of the University of Nebraska, College of Medicine, assisted by Fellows of The American College of Allergy and the American Academy of Allergy.

INTERNATIONAL SYMPOSIUM

The Eighth International Symposium on "The Mechanisms of Hypersensitivity" will be held in Detroit, Michigan, at the Henry Ford Hospital, March 27-29 inclusive, 1958. There is no registration fee.

The twelve individual symposia are: Heterogeneity of Antibodies; Detection of Antibodies in Human Sera; Effects of Antibody and of Antigen-Antibody Complexes on Intact Cells and Whole Organisms; Permeability Factors; Participation of Complement in Allergic Responses; Auto-Antibodies; Delayed Type Hypersensitivity Reactions; Immunologic Unresponsiveness; Tolerance and Rejection of Tissue; Hormones and Allergic Responses; The Role of Mycobacteria in Allergic Manifestations; and Some Factors Modifying the Response to Allergens.

When this announcement was received, approximately one hundred invitations were open. Attendance is by invitation because of the limited seating capacity in the hospital auditorium. Those wishing to attend should write immediately to the General Chairman, Joseph H. Shaffer, M.D., Henry Ford Hospital, Detroit 2, Michigan.

RESIDENCY IN ALLERGY

The Allergy Division of The Jewish Hospital of Brooklyn will have an opening for a Resident-in-Allergy, beginning July, 1958. The salary is open.

A wide scope of both detailed clinical study and basic experimental investigation is offered. Upon completion of the Residency, an In-Patient Staff appointment will be offered, if the obligations of the positions can be fulfilled.

Those interested should contact Dr. Max Grolnick, Attending-in-Allergy at The Brooklyn Jewish Hospital.

THE PSYCHOPHARMACOLOGY SERVICE CENTER

The Technical Information Unit of the Psychopharmacology Service Center of the National Institute of Mental Health at 8719 Coleville Road, Silver Springs, Maryland, has been established as a clearing house for information with bibliographic and reference service and critical and analytic reviews of special topics in the field.

Not only will there be accessible a collection of the literature on the pharmacological, clinical, behavioral and experimental aspects of the ataractic, psycho-mimetic and centrally acting drugs, but the Center invites those working in any aspect of the field to send to it three copies of any paper dealing with any aspect of this type

of study. Restrictions placed by the author upon the use of his work will be observed.

The Center will accept pre-publication manuscripts, reprints, progress reports, abstracts, mimeographed reports and outlines of work in progress. Allergists working with ataractic drugs need no special invitation to help enlarge the scope of the collection or to make use of the facilities available.

PENNSYLVANIA ALLERGY ASSOCIATION

The annual spring meeting of the Pennsylvania Allergy Association will be held in the Brunswick Hotel, Lancaster, Pennsylvania, on May 1, 2, 3 and 4, 1958.

The Board of Regents meeting will be held on Thursday, May 1, 1958, at 8:30 p.m., in the Brunswick Hotel. The scientific meetings are as follows:

Friday, May 2

Morning Session—9:00 a.m.

"The Physiologic Basis for the Action of ACTH in Human Beings" and "The Therapeutic Use of ACTH in Human Disease."—Films from the Armour Laboratories.

"Clinical Sensitizing Properties of Commercial Products."—STEPHEN D. LOCKEY, M.D.

"Procedures and Drugs of Value in the Treatment of Intractable Bronchial Asthma".—ETHAN ALLAN BROWN, M.D.

For the Ladies—9 a.m. to noon: Visit the DeSaegar Mill to see fabrics from all over the world.

Afternoon—1:00 p.m.

Tour of John Wyeth Laboratories, Marietta; a box lunch will be served on the bus trip.

Evening—7:00 p.m.

Auction and Pennsylvania Dutch Program.

What will your donation be, an antique article, a product of your handcraft or hobby, books or other?

Saturday, May 3

Morning Session—9:00 a.m.

Business Meeting

"Pulmonary Function Studies and Their Value in Bronchial Asthma."—RICHARD T. CATHCART, M.D.

"The Prophylaxis of Allergic Disease in Infancy and Childhood."—JEROME GLASER, M.D.

For the Ladies—10 a.m. to noon: Accessory Fashion Show at the "House of Mary Sachs."

Afternoon—1:00 p.m.

Lunch at the Old School House, Penryn. An Amish-style meal to be served by Amish women. Tour of the Amish House and countryside.

Evening—6:30 p.m.

Cocktail Party, Banquet and Dance.

Sunday, May 4

Morning Session—9:00 a.m.

"Gastrointestinal Allergy."—PHILIP GOTTLIEB, M.D.

"Some Different Ideas about Allergy."—BELA SCHICK, M.D.

"Analysis of Milk and Its Relationship to the Allergic Infant."—JOSEPH H. FRIES, M.D.

"Practical Management of Bronchial Asthma in Children"—JEAN CRUMP, M.D.

Officers of the Pennsylvania Allergy Association for the year 1958 are:

President.....William A. Reyer, M.D.
President-Elect.....Jean Crump, M.D.
Secretary-Treasurer.....Stephen D. Lockey, M.D.

BOOK REVIEWS

CLINICAL CARDIOPULMONARY PHYSIOLOGY. Editor-in-Chief, Burgess L. Gordon, M.D. 640 pages. 248 illustrations, 32 tables. New York and London: Grune & Stratton, 1957. Price $15.75.

Once upon a time, an allergist could treat a patient with bronchial asthma suffering from any associate disorders with nothing more than a stethoscope and a hypodermic syringe. We now know that the asthmatic patient, although he may not be wheezing, presents changes in lung physiology which can be measured with some degree of accuracy. Such patients require medication, not for the bronchospasm, but for the return of abnormal physiological changes to normal levels.

The book which is sponsored by The American College of Chest Physicians, not only discusses normal pulmonary physiology but also describes in detail methods of examining and testing pulmonary function.

Allergists may not be interested in paralytic conditions or constrictive chest disorders which may impair the mechanics of respiration. On the other hand, they will want to read the chapter on Bronchial Asthma written by Maurice S. Segal and Ernst O. Attinger. They will want to know the pulmonary manifestations of collagen diseases as described by Howard A. Anderson and Herman J. Moersch.

The most recent information on emphysema, by Edwin Raynor Levine and Chi Kong Lu, is needed if this disorder is to be treated in accordance with modern techniques.

The reviewer does not agree with what appears to be a minimizing of the anti-allergic treatment of bronchial asthma. There is, on the other hand, an apparent overemphasis on the subject of intermittent positive pressure breathing therapy. Many of our asthmatic patients do not require drugs given by nebulization.

The overemphasis and underemphasis mentioned are not to be regarded as true faults in the point of view expressed but rather as opinions of the authors drawn undoubtedly from their types of practice.

Although few allergists will want to know all of this book, no allergist should remain unfamiliar with those portions which impinge upon his specialty.

1956-1957 Series YEAR BOOK OF DERMATOLOGY AND SYPHILOLOGY, edited by Rudolf F. Baer, M.D., and Victor H. Witten, M.D, 464 pages including index. Chicago: The Year Book Publishers, 1957. Price $7.00.

The present volume comprises papers published between September, 1956, and May, 1957, of which almost a third are of special interest to allergists. The initial review article discusses (p. 61) the treatment and prevention, by endocrine, physical and other therapies, of allergic eczematous contact dermatitis. The next ninety-two pages are devoted to eczematous dermatitis, that is, atopic eczema, urticaria and drug eruptions. In other words, one third of the book is therefore "required reading." Other sections are miscellaneous dermatoses, cancers and precanceroses, fungus infections, infestations, venereal diseases and investigative studies; all of which are well worth quick perusal.

High points of interest include an evaluation of the ataractic drugs in dermatology. The editors say that they "have had the opposite of a calming effect on those physicians who have seen their patients developing drug eruptions and even nonthrombocytopenic purpura due to these drugs."

Many references to "cross sensitizations" in every subdivision on the subject of dermatologic allergy are especially important to those allergists who may not have access to the growing literature in this field.

Among other abstracts of importance is that of Kempe of the University of California at San Francisco who is quoted as saying that he will ship by air express, free of charge, vaccinia immune gamma globulin on receipt of a telegram or telephone message that it is needed for eczematous children accidentally vaccinated.

Gregersen and Barnard discuss the use of cholase, that is human plasma cholinesterase in cholinergic (nonallergic) urticaria.

According to Klauder and Kimmich, contact dermatitis in carrot handlers is not exacerbated following carrot ingestion. Wiseman and Adler treated a patient with cold urticaria in whom prior ingestion of acetic acid was needed to evoke the urticaria response.

Morris reports the occurrence of hives in two patients after six different exposures to ammonia: adding this substance to the fumes of sulfur, formaldehyde, tobacco and derivatives of frying foods as inhalant causes of urticaria.

Bland ascribes cross sensitizations to tetramethylthiuram disulfide as used both in antiseptic soaps and as an accelerator in the rubber industry.

Peck and Palitz show that urea formaldehyde residues in facial tissues for "wet strength" caused dermatitis in three of fifty test subjects and might therefore be a factor in eyelid or circumoral lesions.

An abstract of Hoigne's work describes a new serologic method of ascertaining sensitivity in inhalant food and drug allergy and should send allergists, aware of the limitations of skin tests, to further references if their basic techniques are to rest on a firmer foundation than scratch or intradermal tests.

All in all, this little book chastens the complacent and heartens those who regard the specialty of allergy as a continuous frontier. Day by day the horizen widens, proving allergic mechanisms to be operative in more and more diseases and disorders.

ALLERGIE. Editor: K. Hansen. Twenty-four authors. Third revised and augmented edition. XXIV + 1211 pages. Illustrated. Stuttgart, Germany: Georg Thieme Verlag, 1957. Price $44.50.

This large and beautifully illustrated presentation gives a typical demonstration of the advantages and disadvantages of multiple authorship without careful co-ordination. On the one side, the reader becomes acquainted with different viewpoints and approaches which is all to the good in a subject as complex and often controversial as allergic diseases. But the reader will have to spend considerable time in order to benefit from the information available in this book on any particular question, because he will have to search several places and then correlate the material. The critical reader will find that the quality of presentation is uneven. Some chapters just skim the surface of their subject, whereas others go into great detail. For those interested primarily in the clinical aspects of the subject, this book cannot compare in didactic value with several available in this country. For the American reader, there is the added disadvantage, that he (quite naturally from the viewpoint and experience of the German authors) will find little information on subjects of great importance here, such as allergy to poison ivy and ragweed. The scientifically inclined reader will much regret the skimpiness or lack of references which he would need in order to obtain access to original European writing.

A.J.W.
